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Association *for the* Study *of*
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September, 1922

THE PRINCIPLES UNDERLYING ORGANOTHERAPY AND HORMONOTHERAPY

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BALTIMORE, MD.

Read at the Sixth Annual Scientific Session of the Association for the Study of Internal Secretions, St. Louis, Mo., May 22, 1922.

INTRODUCTION

When we understand definitely what we are trying to do—and by this I mean having rather more than a vague general idea of desiring somehow or another to be of help to a sick person—we are more likely to be successful therapists than if we fumble about without plan in the hope of hitting luckily upon the right remedial agent. Much of our therapy is, it is true, empirical rather than rational, but we should know when we are working empirically and why, and we should strive to provide for our methods of treatment an ever more rational basis. We should, in other words, plan our treatments as far as possible in accord with *principles,* or *laws,* that we believe to be well established, or that seem likely to become so. There prevails a widespread feeling that many practitioners are making use of endocrine products in therapy in an indiscriminate and haphazard way, taking no trouble to ask themselves in a given case why the administration of such products may be indicated,

but administering glandular substances or derivatives, and especially "mixed products," in various abnormal states merely because advertising matter strongly commends their trial. In how far this feeling is justified by the facts, I do not know, though I fear that it is, at least to some extent, well founded. An extravagant use of these products must be hard to resist at a time when almost every layman has had his interest aroused in one way or another in the internal secretions, when even a considerable proportion of physicians hug the fallacy that because the myxoedematous child is backward mentally therefore most cases of mental deficiency can be cured if only the particular hormone that presumably has been lacking be administered, and when consultants are daily besieged by both laymen and physicians with requests to examine a great variety of patients who "surely must have something wrong with their glands." The situation is not at all surprising, considering the central place that in normal and pathological physiology, the endocrine activities have come, and rightly, to occupy. Giants and dwarfs, Basedowians and cretins, acromegalics and obese monstrosities, as well as eunuchs and pseudo-hermaphrodites, are the victims of endocrine disharmonies. Many normal functions—visceral, neural, mental, metabolic—are demonstrably dependent upon certain incretions that are manufactured in and dispatched from the endocrine organs. An excessive production, a deficient production, or a perverted product may give rise to serious pathological states that sooner or later become manifest in recognizable clinical syndromes. Attempts to follow the trail back from the abnormal clinical picture through the altered structures and functions of the several bodily systems to the chain of hormonopoietic organs and beyond are laudable, but how difficult! Still, thanks to the steady, faithful work of clinicians, pathologists, experimental physiologists and biochemists, endocrinology is gradually being placed upon a firmer basis and we can begin to discern the single links in some of the pathogenetic chains. As a result of such work, a few principles useful as a guide to therapy can be clearly stated.

THE PRINCIPLE OF SUBSTITUTION IN ENDOCRINE DEFICIENCY

According to this principle, the therapist substitutes for deficient production of an endocrine product by a patient (1) an

organ derived from another person or from an animal that will steadily yield that product to the body of the patient (organ-transplantation), or (2) fresh or dried glandular substance derived from animals, or (3) the supposed active principle of the gland concerned, extracted from the glands of animals, or prepared artificially by the manufacturing chemist.

Some of the greatest triumphs of therapy have been due to the application of this principle of substitution. I need refer only to our ability to control myxoedema and cachexia thyreopriva, either (1) by organ transplantation or (2) by administration of thyroid substance or thyroxin. Attempts at substitutive therapy in hypophyseal, parathyroid, suprarenal, gonadal, and pancreatic endocrine insufficiency have been less successful, though for each gland certain results have been achieved that encourage further work in the hope of discovering methods that will be more efficacious than any yet devised. The work of Toronto investigators on diabetes seems at this moment to be particularly promising.

THE PRINCIPLE OF MILD STIMULATION IN ENDOCRINE DEFICIENCY

The activity of a deficient endocrine organ can sometimes be increased by applying the principle of mild stimulation. We have reason to believe that the normal activity of secreting organs in general (inclusive of the endocrine) depends upon stimuli derived partly from the chemical substances in the blood and lymph, partly from the autonomic nerves. What physicians are accustomed to call "building up the general health," a therapeutic measure that all fall back upon for patients who are not well but whose condition does not yield definite indications for local surgical or chemical intervention, consists in altering the environmental influences (diet, fresh air, sunlight, exercise, massage, rest, situation, including physical and psychical surroundings), in the hope of favorably influencing all the bodily and mental functions. In such a general reconstructive process, the physician applies the principle of mildly stimulating cells by increasing the adequate physiological stimuli that reach them.

Recently the attempt has been made to overcome endocrine insufficiency by mildly stimulating more directly the deficient organ by non-physiological irritants, such as x-rays or radium

emanations in small doses. This form of therapeutic stimulation has been tried in thyroid insufficiency, in hypophyseal insufficiency, in suprarenal insufficiency, and, recently, in insular insufficiency of the pancreas. It is too early, as yet, to judge of the efficacy of this form of treatment. The principle would seem to be a sound one, even though it should turn out to be of limited application.

THE PRINCIPLE OF ORGAN-REDUCTION OR OF FUNCTION-REDUCTION IN ENDOCRINE HYPERACTIVITY

In states of hyperfunction (and sometimes of dysfunction) of an endocrine organ, the therapist applies the principle of organ-reduction, or of function-reduction, often greatly to the benefit of the patient.

An organ may be reduced by partial excision by the surgeon, or by causing necrosis or degeneration of its cells by injections of hot water, by galvano-cautery, by electrolysis, or by intensive radiation with x-rays or radium.

The function of an overactive organ may be reduced by lessening its blood-supply (ligation of vessels; cold applications), by injury short of necrosis by means of x-rays or radium, by electrical treatment, or, sometimes, by a well-devised pharmacotherapy.

These principles of organ-reduction and of function-reduction have been successfully applied in the treatment of thyroid hyperfunction (Graves' disease, etc.), of ovarian hyperfunction (production of artificial menopause in severe menorrhagia and certain cases of puerperal osteomalacia), and of thymus hyperplasia (status thymicolymphaticus) and less successfully as yet in hypophyseal hyperfunction (gigantism; acromegaly) and in suprarenal hyperfunction (either chromaffine or interrenal).

THE PRINCIPLE OF UTILIZING HORMONES AS PHARMAKA IN THE TREATMENT OF CONDITIONS NOT NECESSARILY DEPENDENT UPON HYPOFUNCTION OF THE ENDOCRINE ORGANS THAT MANUFACTURE THEM

Physiologists, pharmacologists and experimental therapists are rapidly accumulating data that throw light upon the selective power of the several known hormones upon particular physiological mechanisms. The newer knowledge thus gained not

only gives us a better appreciation of normal endocrine functions than we formerly possessed, but in certain instances has placed in our hands for particular conditions new remedies whose favorable action could scarcely be accounted for by the assumption of a mere substitutive therapy that compensated for an endocrine deficiency. Thus the astonishing effects of epinephrin injections in bronchial asthma, and the equally remarkable results obtainable by pituitrin injections in diabetes insipidus and in dynamic ileus, to say nothing of its action on the uterus, are examples of the application of a new principle that may be capable of an unguessed extension. Is it not likely that, as medical science advances, we shall learn how to use as remedies a host of substances that we now know only as body-constituents of complex chemical constitution?

CONCLUSION

There are a number of other principles that endocrinologists are applying in their efforts at organotherapy and hormonotherapy. I should have liked to refer, had time permitted, to the principle of existing organ-deficiency as a favorer of successful organ-transplantation, to the principle of reciprocal interdependence of the endocrine organs as a basis for a stimulating therapy on the one hand and for an antagonistic therapy on the other, and to the principle of a multiglandular therapy in the management of generalized sclerosis of the endocrine organs. Time will not permit of this, however, and, moreover, as we know as yet but little regarding the last-mentioned principles, it seemed best to lay emphasis upon the principles that are better understood and are more generally applicable.

If physicians when studying the endocrinopathies will endeavor to make complete diagnostic studies before they plan their therapy, and if, when deciding upon treatment, they will keep in mind the therapeutic principles that may legitimately be applied in the present state of our knowledge of endocrinology, making use of the scientific imagination in devising better methods of application, they will be doing their best to secure all that is obtainable for their patients, to help their colleagues in the profession by extending knowledge and improving technique, and to protect their fellows as well as themselves from any deserved opprobrium.

A CHINESE CRETIN TREATED WITH NATIVE MEDICINE

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Cretinism among the Chinese apparently is not common. Annual reports from 14 hospitals in China, giving diagnoses of 33,000 in-patients, do not record a case of this disease.

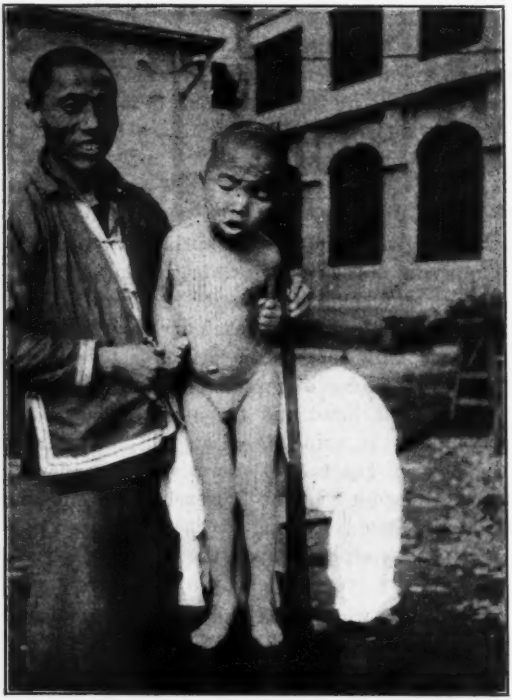

Fig. 1. A Chinese cretin, aged 17, after five weeks of thyroid medication. The attendant holds a meter stick.

The cretin here reported was a Chinese boy of 17 years who was sent to the Peking Union Medical College Hospital by Dr. Bryan-Brown of the British Legation. There was no family history of goiter. He looked like a child of four or five years.

He could not walk without support and could answer only simple questions. His temper was uncertain. When displeased he squealed like a pig. He weighed 46 pounds and was 39 inches in height. His head was disproportionately large, eyes wide

Fig. 2. The same patient as in Fig. 1, after four months of intermittent medication consisting of turtle shell, tiger bone, deer horn and thyroid. The Chinese doctor holds a meter stick.

apart, mouth open, lips thick, skin dry, and abdomen protruding. He had no axillary or pubic hair and the genitalia were infantile. There was persistent flexion of the wrists and fingers, in a position characteristic of tetany. Roentgenoscopy showed a bony development corresponding to about eight years. His blood Wassermann was negative, differential leucocyte count normal, blood pressure 85-60. Determination of the basal metabolic rate was not possible.

For a month before entrance the patient had been taking

three grains of dried thyroid gland a day without noticeable improvement. For the month that he was in the hospital he was given six grains daily. The resulting increase in metabolism was shown by an increase of the average pulse rate from 90 to 115, and minimum temperature from 97 to 98.6 degrees, by a loss of nine pounds in weight, and by a greatly increased output of urinary nitrogen and creatinin. Determinations on the urine were made by Dr. B. E. Read. Fig. 1 is a photograph taken at the end of five weeks of thyroid medication.

In spite of increased food intake the child continued to lose weight. He showed little or no mental improvement, and his father insisted on taking him home.

About four months later we were told that the boy was being treated by an old style Chinese practitioner and had shown remarkable improvement. Through the good offices of this Chinese doctor we were able to bring the boy, who lived in a nearby town, into the hospital for further observation. A photograph (Fig. 2) was taken of him and his doctor at this time. Examination showed that since discharge he had gained about 12 pounds in weight and three inches in height. His genitalia were more fully developed and the tetany-like contraction of his hands had almost disappeared. His father had taught him some acrobatic tricks and was greatly pleased with the physical and mental progress which he thought his boy had made. The medicine which the doctor prescribed consisted of a mixture of powdered turtle shell, tiger bones and deer horn. He had taken ten large doses of this, costing the equivalent of a laborer's wages for two months. During a part of the time he had also taken thyroid tablets given to him when he left the hospital. According to report, the Chinese doctor had gained considerable local fame for succeeding where the foreign doctor had failed.

McCarrison makes the statement (personal communication to Dr. J. C. Aub) that cases of cretinism with parathyroid deficiency do not improve on thyroid medication alone. In this Chinese boy parathyroid deficiency was suggested by the characteristic position of the hands. The question occurs, whether it is possible that the calcium in the bone prescribed by the Chinese doctor, supplemental to the thyroid gland given by us, produced a growth in bone and in genitalia and a quickening of mentality not secured by thyroid alone.

AN APPRAISAL OF OVARIAN THERAPY.*

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INTRODUCTION

An appraisal of ovarian therapy, or of any other subject, must of necessity be tinctured with the personal element of the appraiser, so that it represents merely the point of view of an individual, based on such knowledge of facts as he may happen to possess. It presents more difficulty than does a mere survey of the literature, from which it differs to the same degree that the critique of a book differs from a mere synopsis of the book's contents. An accurate evaluation of such an undeveloped branch of therapeutics as that which forms the subject of this paper presupposes a finer judicial sense than the present writer can lay claim to. It is not easy to steer safely and sanely between the Scylla of over-enthusiasm and the Charybdis of undue skepticism. I may anticipate somewhat by saying that, of the two, Scylla looks much more dangerous to me than does Charybdis, to which I shall therefore be rather partial. One may be ever so enthusiastic as to future possibilities and yet be forced, in all honesty, to present a rather depressing picture as to what has actually been accomplished up to the present time by the therapeutic use of the various forms of ovarian extract. Since this paper is to be an appraisal and not a complete survey of the literature of the subject it can be kept within the limits of considerateness by presenting only the personal reactions of the writer, after a fairly abundant clinical experience and a reasonable familiarity with the literature of the subject.

HISTORICAL

The first attempts along the lines of ovarian therapy, so far as I have been able to find, were made at the Landau Clinic, in Berlin, in 1896, as detailed in several papers emanating from

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this clinic in that year. The first of these, by Mainzer (1), gives the credit for the idea to Theodore Landau. The method was obviously suggested by the good results which had been obtained from thyroid therapy, even at that time. Mainzer reported the case of a girl of 23 in whom double salpingo-oöporectomy had been performed for extensive pelvic inflammatory disease, and who had developed severe vasomotor symptoms, which failed to respond to all ordinary methods of treatment. Ovarian therapy was then resorted to. Before the beginning of the treatment the patient averaged about twelve severe attacks per day of flushing of the head, giddiness, sweats, etc. Within three days of the beginning of the treatment, the attacks had diminished to a daily average of five. To make sure that the effect was not merely psychic, the patient received a substitute (scraped meat) on the seventh and eighth days, and felt much worse. On again being given the ovarian substance, improvement was again noted, to be followed by retrogression when the substitute was again given on the fourteenth day.

The preparation employed was the fresh ovarian substance obtained from the cow or sow. After careful removal from the animals, the ovaries were allowed to dry for twelve hours at a temperature between 60° C and 70° C, and then administered in the fresh condition. It was not long, however, before the substance was prepared commercially in convenient tablet form.

For a time the only preparation employed was that obtained from the entire ovary, but with the recognition of the corpus luteum as an incretory gland there were begun attempts to treat various conditions with preparations made from corpus luteum alone. Fraenkel (2) himself, the foster father of the general corpus luteum theory, reported good results in a small series of cases.

In 1904, Burnam (3) published the results of his observations on the use of fresh corpus luteum substance from the sow in the treatment of various gynecologic conditions. His results were so encouraging that a fresh impetus was given to this form of therapy. The literature of recent years abounds with reports concerning the use of both ovarian and corpus luteum substances in a great variety of conditions, as will be discussed below.

PHYSIOLOGICAL BASIS OF OVARIAN THERAPY

The known facts as to the physiological function of the ovary are sufficient to supply a logical basis for the general idea of ovarian therapy. Most of this evidence has been obtained, as with so many of the other endocrine glands, by studying the effects of ovariectomy in both human beings and lower animals. Much less impressive has been the evidence secured along positive lines, i. e., by studying the effects of feeding or injecting ovarian extracts of one form or another.

Whatever the relationship of the ovaries to the remainder of the endocrine chain may be, they are universally accepted as the organs which are directly responsible for the occurrence of menstruation. Furthermore, their removal is often followed by certain vasomotor and metabolic disturbances quite similar to those observed at the normal menopause. Again, the studies of Fraenkel, followed later by those of Meyer, Schroeder, Ruge, and others appear to have demonstrated conclusively that the corpus luteum is the element in the ovary which is responsible for the occurrence of the menstrual cycle, and the chronological relationships of the ovarian, endometrial, and menstrual cycles have been quite satisfactorily worked out. Far less satisfactory is the evidence concerning that function of the ovary concerned with general metabolism, that having to do with a possible influence on the growth and development of the generative tract and that pertaining to a protective influence on the early embryo. This is not the place to review these various questions, my object being merely to show the limitations of our present knowledge on these subjects as compared with the many therapeutic uses to which ovarian extracts are put.

PHARMACODYNAMIC ACTION OF OVARIAN EXTRACTS

Interesting observations have been made within recent years as to the effects of these extracts upon the genital organs. Adler (4) by the injection of watery ovarian extracts, and of ovarin (Pochl) into virgin rabbits and guinea pigs was able to produce changes similar to those normally occurring at the oestral epoch. Similar, though much less marked, changes were evoked by watery extracts of corpus luteum. Adler furthermore states that by administering ovarin he was able in two

cases to bring on the menstrual period, while the uterine mucosa showed the typical menstrual histological changes.

Schickele's experiments (5) were perhaps even more striking. He injected extracts of ovary and of corpus luteum into castrated animals and was able to demonstrate within two or three weeks a pronounced redness and swelling of the vulva and vagina, with the appearance of a mucous discharge. Similar observations have been made by Marshall and Jolly. Aschner likewise obtained results with ovarian extracts while the use of corpus luteum gave negative results.

All the work thus quoted was based upon the use of aqueous or weakly alcoholic extracts of the ovary or the corpus luteum. To Iscovesco (6) belongs the credit of attempting to separate the active principle by the use of solvents which would not leave behind the lipoids, for he believes that the latter represent the biologically active principle of the secretion. Iscovesco's work marks the beginning of a really scientific effort to isolate the active principle of the ovary. He divided these lipoids into two groups, the homostimulating and the heterostimulating, depending up on whether they act only upon the organ from which they arise, or also upon the other organs. In the former group he places the secretions of the ovaries and of the testes. He was unable to distinguish any difference between the lipoids of the ovarian and corpus luteum extracts either physiologically or therapeutically. For the rather complex details of his method of preparation I shall refer the reader to his various papers.

A somewhat similar technique led Fellner (7), in 1912, to the isolation of a substance which produced striking effects upon the uterine musculature, epithelium and glands. These effects were noted even in castrated animals. Perhaps the most thorough and most suggestive work of this sort, however, has been that of Herrmann (8), published in 1915. This author believes that he has isolated the active principle of the ovary, and the illustrations accompanying his article, showing the effects of injection of the preparations, are certainly quite impressive. The technique he employs is a very complicated one, but its end result, Herrmann believes, is the isolation of the active lipoid principle, which he believes is contained in the corpus luteum. Incidentally he finds that the placenta contains identically the same principle. The lipoidal substance which he

has worked out shows a high grade of activity, but whether it is itself the active principle, or whether it merely contains the latter in a concentrated form, can not yet be definitely stated. Herrman's claim to priority in this matter has been challenged by Fellner, and an interesting controversy on this point has been waged in recent numbers of the Zentralblatt für Gynäkologie.

Finally, mention may be made of the investigations of Seitz, Wintz and Fingerhut (9), who separated from the corpus luteum two distinct substances which they call luteolipoid and lipamin. The former has an inhibitory action on the menstrual function and is found in large amounts in the later stages of the corpus luteum. The lipamin, on the other hand, is said to stimulate the growth of both the internal and external genitalia in animals, while its subcutaneous injection in amenorrheic women will bring on menstruation. Both of these substances have been prepared commercially in Germany. It may be added that the methods employed by Seitz, Wintz and Fingerhut in the preparation of these substances have been criticized by Herrmann, who believes that the results obtained were incorrectly interpreted.

Aside from any possible specific effects of the administration or injection of ovarian extracts other phenomena have been noted which may have some bearing on the therapeutic employment of these substances. For example, Federoff, in 1899, found that an important effect of ovarian extracts was a slowing of the heart and an elevation of the blood pressure. The latter observation, however, is contradicted by most subsequent investigators. Goñalons (10) finds that "immediately following the injection of 20 cc. of maceration or decoction of gravid corpus luteum, there is a rapid hypotension of 50, 60 or even 80 mm. of mercury. The pressure falls rather rapidly, cardiac pulsations are generally considerably weakened, and there are sometimes in the first moments deep convulsive respirations. After 1, 2 or 3 minutes the pulsations strengthen and the pressure rises. This is relatively rapid at first. After 5, 7 or 10 minutes, sometimes more, the pressure returns to normal; at other times it persists a little diminished." Goñalons states that the same general results, though less marked, are observed if a maceration or decoction of the ovary is used. He finds,

furthermore, that both ovarian and pregnant corpus luteum preparations produce a tonic contraction of the uterine muscle, with also an increase of the rhythmic contractions. His results are quite similar to those obtained by Barry. Stickel, on the other hand, states that the intravenous injection of ovarian extract yielded no results. Bell and Hick also got negative results from ovarian extracts upon the virgin uterus, but noted a stimulating effect upon the pregnant organ. Adler found that the administration of ovarian and corpus luteum extracts usually produces an increase of blood pressure, while Schickele obtained just the opposite effect, a fall in the blood pressure.

Mention may also be made of the experiments of Matsumoto and Macht (11), who found that "in all cases" both ovarian and corpus luteum preparations produced a powerful stimulation of the contractions and an increase in the tonus of the excised uterus. This effect was more pronounced with the corpus luteum extracts than with the ovarian. The authors very properly, however, warn against the assumption that these effects are specific in nature, for stimulation of the uterus was produced by practically every other gland or organ with which they experimented. They recommend as a test for corpus luteum preparations, the determination of this effect on the vas deferens of the rat, which they found to be very sensitive to the preparation. This test, as will be noted below, has been adopted by at least one manufacturing house, although its value as an index of specific therapeutic activity seems very questionable.

THE COMMERCIAL PREPARATION OF OVARIAN EXTRACTS

This brief résumé of the physiology of the ovary and of the pharmaco-dynamic action of its extracts leads to the question as to whether or not manufacturers have kept pace with the progress of laboratory investigators along this line, slow as this has been.

I have recently written to three of the largest manufacturers of ovarian extracts in this country, with the request that they supply me with a detailed account of the method employed in the preparation of the various forms of ovarian extract. This request was very courteously responded to by each of these manufacturing houses. I am sure that many of you will be

interested in these communications, which are therefore included below.

Manufacturer A: "We prepare our corpus luteum product from hog ovary glands, selected, collected and shipped in accordance with the following specifications:

"The hog ovary glands are taken only from Government inspected animals. Immediately after the animal is killed, the glands are placed in a container containing crushed ice, during the period of collection. They are then removed to a cooling room and spread out in layers not more than an inch in depth, and are allowed to remain over night, until all animal heat is removed. These glands are then placed in a Sharp freezer and are frozen solid. They are immediately shipped to our plant, where they are thawed out and the skins and tissue are separated by mechanical means and the corpus luteum is reduced to a pulp. This pulp is placed on drying pans in a vacuum drier and the product is reduced to dryness at a temperature below animal heat, approximately 90° F. This material is powdered and compressed into tablets.'

"At no time during the process of preparation is the material subjected to a temperature above animal heat, nor is it treated with solvents or chemicals, or modified in any way. It, therefore, represents as nearly as possible, the fresh animal gland.

"The whole ovarian material is prepared in the same way, with the exception that the entire gland is reduced to a pulp and the tissue and skin is not separated from the corpus luteum.

"Ovarian residue is the separated tissue and skin obtained during the process of preparing the corpus luteum. Otherwise, the ovarian residue is prepared in the same manner as is corpus luteum.

"The soluble extracts are prepared by extracting the powdered gland with an aqueous solvent and treating the clarified solution with protein precipitating agents, filtering off the solution, concentrating in vacuo, after removing every trace of the precipitating agents, until 1 cubic centimeter represents the water soluble extractive from 2 decigrams of the powdered substance.

"These products are also standardized physiologically by the Macht-Matsumoto vas deferens test, Journal of Urology, April, 1919."

Manufacturer B: "We manufacture Corpus Luteum and Ovarian Substance from the glands of both hogs and cattle. The corpora lutea are removed from the glands and the remaining portion of the glands, sometimes referred to as residue, is mixed with glands that are without corpora lutea and sold as ovarian substance in powder and in tablets.

"Our method of handling the glands is to take them while perfectly fresh, free them from fat and connective tissues, mince finely and desiccate in vacuo at a temperature ranging from 85 to 105 degrees F. This low temperature prevents coagulation of the proteids and insures full therapeutic activity. After the glands are desiccated they are defatted and powdered.

"We offer the two preparations referred to in powder and in tablets. We do not make any liquid preparations of either the ovarian substance or the corpus luteum."

Manufacturer C: "The whole ovaries, as dissected from the animal in the packing house, are frozen solid and sent to us in this form so that they reach us without decomposition. The slightest evidence of any decomposition, which is best shown by the odor, is sufficient to cause us to throw them away, as we cannot take any chance on preparations of this kind. On the whole, such glands reach us in excellent condition. As a matter of fact, we do not think they stay in frozen state for great lengths of time, but are shipped to us quite fresh and are frozen merely to be certain of their preservation during whatever time elapses between their collection and manufacturing work in our laboratories.

"They come both from cattle and from hogs. On reaching our laboratories they are first carefully inspected, then washed, and any extraneous tissue removed. Now if it is decided to make desiccated whole ovarian substance, the entire gland is ground to a fine pulp and carefully dried at a low temperature in vacuum drier. The dry material is then ground to a fine powder and stored perfectly dry in air tight containers, preparatory to its further use in capsules or manufacture of soluble extract.

"For the preparation of desiccated corpora lutea, these characteristic yellow bodies are carefully dissected from the rest of the tissue and then ground and dried in vacuum in the same manner as above. The portion of the glands which remains after dissecting out the corpora lutea is likewise dried in the same manner and constitutes what we designate as ovarian residue.

"While we know, from such experimental work as has been done, that ovarian substance and corpora lutea both produce very pronounced effects upon human beings, and are exceedingly useful in the treatment of a variety of diseased conditions, yet our knowledge of the active principles contained in these gland products is practically nil.

"Working somewhat along the same lines as that for the preparation of the active pituitary solution from the pituitary gland, we have developed some soluble extracts of ovarian residue, whole gland and corpora lutea. We have used for this purpose a process, whose general outline is as that given by the U. S. Pharmacopoeia for the preparation of Extract of Pituitary Gland. In short, it involves the extraction of the desiccated gland (and the finer it is ground the better), with water slightly acidulated with acetic acid; the coagulation of proteids which can be coagulated by heating to just below the boiling point of water, and careful evaporation in vacuum so that the final solution will represent about 5 grains of desiccated gland in each cc. This would be equivalent to approximately 30 grains of the original fresh glandular substance.

"It is rather an odd characteristic of these solutions that on chilling they frequently solidify to a transparent jelly. It seems that what

soluble organic matter is dissolved is of gelatinous nature, and though present in the liquid to an extent of not more than about 4% will rather easily gelatinize, especially if the solution is kept in a refrigerator.

"These solutions, as we handle them, are then sterilized by filtering, first through a Berkefeld and later through a Pasteur filter, and immediately filled into ampoules.

"We have convincing clinical evidence that a solution so prepared does possess to a remarkable extent the activity of the original desiccated gland—but we have a long way to go yet before we can say exactly what is the nature of the active principle that is so dissolved, or how much of the organic substance appearing in the solution is really active, and how much may be merely traces of inert material that necessarily accompany it."

From these letters it will be seen that the general method employed is about the same in the case of these three manufacturing houses. It is true that there are certain differences in the method of drying the product, as well as in the matter of defatting or degreasing. Manufacturer B states that "after the glands are desiccated they are defatted and powdered." No mention is made as to how the defatting is done, or as to what, if any solvents, are used for this purpose. In view of the work of Hermann and others, as described above, this may be a matter of no little importance.

Although I have not written to all the manufacturers in the United States, I understand that practically all of them resort to degreasing processes. This makes a finer and smoother product from a commercial viewpoint, but there can be little doubt that it diminishes the therapeutic effectiveness of the preparation.

There are other possibilities of error in the manufacture of these preparations. The collection of these glands at the abattoirs is done by employees of the latter. In spite of the training, these men receive in the selection of material which will conform to the specifications of the manufacturers, mistakes frequently occur, although manufacturers appear to make a real effort to check up the material after it reaches them.

The question of dosage of these various preparations is still in a very unsatisfactory condition. Unlike the posterior pituitary substance, the thyroid, and the adrenal substances, there has as yet been no effort at standardization, so that, when prescribing these substances, we must proceed on the basis of what

the manufacturer tells us concerning his own product, *i. e.*, just how many grains of fresh or dried substance each tablet or capsule represents, and what the average dosage should be. This puts us in a rather unenviable position, with no relief in sight until some satisfactory basis of standardization is worked out. The physiologic test of Matsumoto and Macht, which at least one firm has adopted, impresses one as of doubtful value. While it may furnish a good index of the effect of the preparation in stimulating contractions in the excised vas deferens of the rat, it is by no means certain that it can be interpreted as an indication of the amount of specific corpus luteum secretion present in the product.

Equally unsettled is the question of whether the extracts, especially those of the corpus luteum, should be prepared from the ovaries of pregnant or of non-pregnant animals. Some manufacturers emphasize, as a special advantage of their product, that it is derived only from pregnant animals. Osborne (12), on the other hand, believes that, "for ordinary clinical purposes the mixed preparations from both pregnant and non-pregnant animals seem perfectly satisfactory." If the word "equally" be substituted for the word "perfectly" in the latter sentence, I should be willing to subscribe to it. It seems certain that there must be some difference between the effects of the corpus luteum of menstruation and that of pregnancy, but it is useless, in the present state of our knowledge, to speculate on the exact nature of this difference, and how it effects the pharmacologic action of the corresponding extracts.

FORMS OF OVARIAN EXTRACT AVAILABLE

A number of forms of ovarian extract are available commercially, so that one may prescribe according to one's views on the relative importance of the corpus luteum and other elements in the ovary. Extracts of the entire ovary, as well as those of the corpus luteum, are now procurable in a number of different forms, viz., tablets, capsules, powder, and even solutions suitable for hypodermic administration. Of the solid preparations, it probably makes no great difference whether one employs the powdered form, capsules, or the compressed tablets. Osborne considers that the substance is best administered in the form of a powder, in capsules of the desired dosage. With regard to the

soluble forms of extract, the evidence would seem to indicate that they are far less efficacious. This statement is made on the basis of such experimental work as that of Aschner, Herrmann and others, on the probable lipoid nature of the active constituent of the ovary. There is no really worth while evidence that a mere aqueous extract of either ovarian or corpus luteum substance contains any of the specific secretion of the organ, and, in fact, the evidence is opposed to this view. These extracts are now prepared by practically all the commercial houses, and they have achieved a wide vogue. Aside from the literature of these manufacturing houses, there is surprisingly little to be found as to the therapeutic results which may be expected from them. Recently, it is true, a number of reports have appeared with regard to the hypodermic use of aqueous corpus luteum extracts in the treatment of the vomiting of pregnancy. The few favorable reports on this subject, however, are of no particular scientific value, as will be discussed later in this paper, and it is quite possible that these preparations are inert.

The use of "ovarian residue" was recommended in 1919 by Graves(13). This preparation is made from that portion of the ovary remaining after removal of the corpus luteum. The reasons advanced for the use of this substance are not convincing, especially the importance attached to the so-called interstitial cells, which do not exist in the human non-pregnant ovary. Furthermore, the few reports of the clinical results which it has given are not especially convincing.

A rather disquieting development of recent years is the question which has been raised by Köhler (14), Esch (15) and others as to whether, with hypodermic ovarian therapy, we are actually concerned with the specific secretion of the ovary—or corpus luteum, as the case may be—or whether this form of treatment is merely a form of non-specific protein therapy. Esch emphasizes a fact which must have impressed all those who have been interested in ovarian organotherapy, *i. e.*, that the same extracts are recommended in diametrically opposite conditions, and that numerous satisfactory reports as to the results in these conditions abound in the literature. This is especially true of extract of the corpus luteum, which is recommended in such antipodal conditions as amenorrhea and excessive menstruation. The former is commonly looked upon as indicative of a

hyposecretion of the ovary, either primary or secondary; the latter, in its purely functional forms, as probably due to hypersecretion of the ovary.

As every one knows, corpus luteum preparations have been used for many years in the treatment of amenorrhea and scanty menstruation, with varying degrees of success. The foundation of this therapeutic theory is, of course, to be found in the Fraenkel-Born theory of the corpus luteum causation of menstruation. Numerous reports are likewise to be found as to their employment in menorrhagic conditions. This method of treatment was probably at first purely empiric. When the function of the corpus luteum became better known, there were many who looked upon this structure as an inhibitor rather than a cause of menstruation. Hence there was some logic in the use of corpus luteum extracts in cases of uterine bleeding. The truth, of course, is a combination of the two divergent points of view. Menstruation cannot occur without the corpus luteum, which causes the hypertrophic changes of the premenstrual period. On the other hand, the actual bleeding of menstruation presupposes a cessation of this upbuilding function of the corpus luteum, as a result of the advent of some new factor, perhaps associated with the death of the ovum given off at the preceding ovulation.

Esch quotes the apparently paradoxical results obtained in various forms of menstrual disorders by the use of ovarian and corpus luteum preparations, and shows that this applies also to the results obtained by preparations from the pituitary body.

To make a long story short, Esch urges that the effects obtained by the parenteral (intramuscular) administration of the various forms of ovarian extract are probably of non-specific character, and that they represent, as a matter of fact, only a form of protein therapy. To substantiate this view, he treated a series of cases by the intramuscular injection of either breast milk or certain proprietaries (Aolan and Caseosan) of albuminous nature. His results were certainly as good as, or better than, those to be obtained with the use of organ extracts. This was particularly true of the cases of excessive menstruation. For his detailed results I must refer the reader to his two recent papers.

Enough has been said, I am sure, to make it plain that this

new aspect of the problem opens up many interesting possibilities. It is rather discouraging, after a quarter of a century of ovarian therapy, to have so fundamental a question as to its validity raised. The theory of protein therapy of this sort is that the effects are produced by the general stimulating action of the split products of the proteins along various lines—gland (and endocrine) activities, muscular action, etc. This work does not, apparently, attack the rationale of the ingestion method of ovarian therapy, except in so far as it creates doubt as to the presence of any of the specific secretion in the various commercial preparations commonly employed.

It is too soon to pass judgment on the correctness or incorrectness of these recent investigations. They strike a blow at the very foundation of ovarian therapy and emphasize again the importance of demonstrating beyond doubt the active principle of the ovary.

On the other hand, it may well be urged that the isolation of this principle should not be considered an essential for success in ovarian therapy. The results obtained from thyroid organotherapy were brilliant many years before the discovery of thyroxin by Kendall. A careful analysis of such a method of manufacture as that outlined by Manufacturer A in the above quoted letters fails to show any important defects. It would certainly seem that if there is any active principle in the ovary or corpus luteum, it would be kept intact by this method, which gives us the entire substance, without the removal of the slightest constituent by means of degreasing or other processes. If the whole product gives unsatisfactory results, is it probable that we would get better results from a purified ovarian extract, except perhaps in a quantitative sense? It would certainly seem that a carefully manufactured product including the entire corpus luteum substance, would contain the lipoid substances to which such importance has been attributed by recent workers. The commercial preparation of extracts by methods similar to those employed in the laboratory by Herrman and others, methods which aim to get out the lipoidal constituents, would be a rather costly process. Perhaps it might be more feasible to make an oily extract which would contain many of these lipoid principles.

From the fact that the results of ovarian therapy are so unconvincing even with the best commercial preparations, I am

inclined to believe that the real trouble is more deeply situated. We cannot even be sure that all the ductless glands have an appreciable amount of the active principle stored up within their cells. This doubt, it has always seemed to me, would apply with especial force to the ovary, which has to do with such purely vegetative functions as menstruation and reproduction. Or, the specific secretion may be present in some antecedent form which is in itself inactive. Finally, there is the possibility that it may lose its activity with the death of the tissue, or that it is destroyed by some of the essential steps in preparation, such as the drying or pulverizing process.

INDICATIONS AND RESULTS

It is unfortunate that most of the indications for ovarian therapy are of the subjective variety. Clinical results alone are obviously less reliable than would be the case if it were possible to control them by animal experimentation. The more conservative element in the medical profession has within recent years frowned upon the practice of proprietary medicine manufacturers of bolstering up their claims by means of "clinical reports" as to the therapeutic virtues of their preparations. However absurd these claims might seem to be, the graphophonic detail man could meet every objection by the stock argument that "after all, doctor, it is results that count." As if equally brilliant results could not be obtained, in many subjective disorders, by patent medicines of the most flagrant sort or by bread pills alone. The only difference between the innumerable patent medicine testimonials found in newspapers and many so-called "clinical reports" is that in the one instance the gullibility of the laity is displayed and in the other the credulity of the equally human medical profession. I trust that these remarks will not be misunderstood, for I am not discounting the unquestioned value of honest clinical observation carried out in a really scientific, truth-seeking spirit. To the clinician we are, as a matter of fact, indebted for some of the most important contributions to endocrinology. For the most part, however, we must look to the laboratory worker for the really substantial advances in this field of work.

Indications: Among the conditions for which ovarian extracts have been recommended may be mentioned amenorrhea,

functional uterine bleeding, dysmenorrhea, infantilism of the generative organs, the vasomotor and nervous disturbances of the menopause, sterility, obesity, repeated abortion, vomiting of pregnancy, pruritus vulvae, kraurosis vulvae, deficient mammary secretion, epilepsy, and Graves' disease. To these might be added quite a number of others even more illogical than some enumerated. Only a few of these have any claim whatsoever to serious consideration.

Amenorrhea: The use of ovarian extracts would appear to be a rational procedure in the treatment of amenorrhea of the so-called functional type, especially that seen so commonly in association with the adiposo-genital syndrome. I have treated many such cases with extract of whole ovary and many with corpus luteum extract, and have not been able to convince myself that the patients have derived any very great benefit. This is especially true when these extracts are given alone, *i. e.*, when they are not combined with pituitary or thyroid extracts. In the latter case, I have at times obtained results which were at least encouraging. My impression, however, is that these same results would have been obtained had the ovarian extracts been omitted, and that the thyroid was the potent element in the treatment.

Aside from my personal experiences, I have been unable to find any reports in the literature which would convince me that this experience has been unique. Indeed, almost the only optimistic reports have been those embodied in the literature issued so generously by manufacturers of these preparations. The German school of gynecologists appears to have replaced ovarian therapy with pituitary therapy in cases of amenorrhea, as evidenced by such recent contributions as those of Köhler, Hofstätter, Fries, Zöppritz, and others.

In spite of the poor results which ovarian therapy gives in cases of functional amenorrhea, it is certainly to be preferred to the less rational, equally unsatisfactory, and more dangerous use of the emmenagogue drugs which have in the past been so popular (the vegetable oils, manganese, etc.). In many instances amenorrhea, in itself, calls for no treatment whatsoever, although it is at times difficult to convince patients of this fact. The laity, and to a less extent the medical profession, still seem to look upon menstruation as a means of ridding the woman's body of

noxious elements. Furthermore, not a few women believe that amenorrhea predisposes to tuberculosis—that if a girl does not menstruate regularly she is likely to go "into decline." For this reason, an important part of the treatment of amenorrhea is to reassure the patient, to enlighten her as to the real significance of menstruation, and to impress her with the innocuousness of its absence, provided the amenorrhea is not secondary to some serious constitutional condition, such as tuberculosis or anemia.

Uterine hemorrhage: I have already referred to the fact that ovarian therapy is used in the treatment of both an absence and an excess of menstruation, and have discussed the reasons for this paradoxical practice. As to the actual clinical results in cases of functional uterine bleeding, especially the hemorrhage of puberty and the climacteric, little of a definite nature can be said. Good results have been reported by a few writers (Schroeder, Flatau, Hannes, etc.), but these reports are so few, in comparison with the great number of unsuccessful, and therefore usually unreported cases, that they must be received very unenthusiastically. The form of therapy which has been perhaps most widely used for this purpose is the intramuscular or intravenous administration of the water soluble extracts. In the light of what has been said above as to the questionable value of these aqueous extracts considerable doubt is thrown upon the occasional reports of good results following their use in cases of uterine bleeding. Certainly uterine hemorrhage, in my own experience, is no less frequently benefited by the use of thyroid or pituitary extracts than by the use of either ovarian or corpus luteum substance.

Menopausal vasomotor symptoms. Here the indication for the use of ovarian extracts of one form or another is good, *i. e.,* it is based on known facts. I believe it can be said that there is a nearer approach to unanimity among clinicians as to the value of ovarian therapy for this indication than for any other. Whether, in the treatment of these disorders, ovarian or corpus luteum extracts actually do "hit the spot," or whether we are here concerned with a great fog of self-delusion on the part of both patients and physicians, it is difficult to determine, through the very nature of the case. The hot flushes, the flashes of heat, and the other characteristic symptoms of the menopause are purely subjective symptoms. They vary much in severity

in different women, and in the same woman at different times. The duration of the menopausal disturbance also varies a great deal, some women being annoyed for only a few months, others for a good many years. It is obvious, therefore, that the greatest caution is necessary in drawing conclusions as to the value of any therapeutic agent for symptoms of this character. Unless I have been greatly deceived, I have seen genuinely good results from organotherapy in this group of cases. The symptoms have often appeared to be diminished, though rarely do they cease entirely. These results have been obtained even when reviewed in the light of such clinical checks as are open to us in the management of cases of this type.

Dysmenorrhea and genital hypoplasia (infantilism, etc.). The only type of dysmenorrhea in which there would seem to be any excuse for ovarian therapy is that associated with underdevelopment of the uterus. The latter condition is probably not a manifestation of primary hypofunction of the ovary. I do not agree with the assertion of Frank (16) that the pituitary has nothing to do with the causation of uterine hypoplasia. There is considerable evidence, both clinical and experimental, that it is concerned. It would be absurd to argue that the existence of such a relation is made doubtful by the mere fact that pituitary feeding does not give results in cases of underdevelopment of the generative organs—just as absurd as to claim that the ovaries have nothing to do with menstruation because ovarian extracts will not bring on menstruation in castrated women. The pituitary treatment, as a matter of fact, would seem to be a logical plan in cases of genital hypoplasia, with or without dysmenorrhea. Since there is also at least a secondary hypo-genitalism in such cases, ovarian extracts would seem to meet a definite indication. The fact remains, however, that the actual clinical results by various combinations of these two organ extracts are negligible, so far as I have been able to learn. I do not believe, however, that the poor results from this method of treatment are to be considered as reflecting upon the correctness of the theory upon which it is based.

The vomiting of pregnancy: In 1916 Hirst (17) suggested the hypodermic employment of the soluble preparation of corpus luteum in cases of vomiting of pregnancy. His view is that "it is not unreasonable to suppose that there is sufficient absorption

from the corpus luteum of pregnancy to account for disappearance of nausea, especially when one realizes that the nausea begins to diminish at the time the corpus luteum has reached its acme of development." This explanation is obviously purely speculative. It is a good example of endocrinology of the less desirable sort. In spite of this fact the treatment based on this idea was gobbled up without question by a profession always hungry for something novel and at least pseudo-scientific. Although Hirst reports eighty per cent of cures in cases of vomiting of pregnancy from the corpus luteum solution, which he now advocates administering intravenously, these figures have not been borne out where the result has been properly checked, as in the recent report of King (18). Rongy and others have likewise reported disappointing results. My own feeling is that the method will soon be thrown into the rapidly growing endocrinological junk heap.

Sterility: The results of the treatment of sterility by ovarian corpus luteum extracts have not been sufficiently good to commend them to most clinicians. Even when an occasional successful result seems to follow, it need scarcely be said that the greatest caution should be exercised in crediting it to the organotherapeutic measures employed. Fallenberg (19) has advocated large doses of the extracts, beginning with five grains a day and gradually increasing until at the end of a month thirty grains a day is being taken. The treatment, be believes, should be continued for one year.

The most successful cases, according to Solomons (20), are those in which menstruation is scanty. These are ordinarily instances of uterine hypoplasia, in which the ovarian therapy is most frequently combined with the administration of pituitary substance. In spite of sporadic and usually unchecked reports of success, good results are not ordinarily to be looked for in the treatment of sterility by ovarian extracts.

Obesity of hypogenital origin: Obesity is frequently observed in cases of hypogenitalism, especially at the menopause or after surgical removal of the ovaries. Here the indication for ovarian therapy would seem quite clear, but it is only fair to say that it rarely yields results unless combined with the administration of thyroid extract, in which case the latter is undoubtedly the potent agent.

Other indications: The numerous other indications for which ovarian therapy has been employed are scarcely entitled to serious consideration. In practically all cases what little evidence there is as to good results is clinical and subjective, and as a rule even this form of evidence is not imposing either in quantity or quality.

GENERAL COMMENTS

In judging the results of ovarian therapy, or for that matter, of other forms of organotherapy, most of us have unconsciously succumbed to the familiar "post hoc propter hoc" error into which it is so easy to slip. In connection with endocrinology some one has given an amusing illustration of the absurdities into which we are so easily led. If the administration of cascara relieves constipation, ought we to assume, inquires this philosopher, that the constipated individual is a sufferer from hypocascarism? Ridiculous though this seems, it represents exactly the method of reasoning employed by many of us when we leave good old mother earth to float dizzily through the cloudbanks of endocrinology. As our former president, Dr. Cushing, said in his address last year, "The Lewis Carroll of today would have Alice nibble from a pituitary mushroom in her left hand and a lutein one in her right, and presto! she is any height desired."

The real stumbling block to success in ovarian therapy, as will be gathered from what has already been said, is a much more material one than that just mentioned, having to do, so to speak, with a condition and not a theory. Nothing can be more certain than that removal of the ovaries brings about a cessation of the menstrual function and frequently the appearance of a characteristic grouping of symptoms. Equally certain does it seem to be that the symptoms of the normal menopause are due to the cessation of ovarian activity. It does not follow, however, that the feeding or the injection of ovarian extracts can replace the normal ovarian secretion, that it can restore the menstrual function and cause a cessation of the menopausal symptoms. The removal of the parathyroids, to select another example, produces tetany and death. The fatal result can not, however, be averted by the feeding of any amount of parathyroid substance.

There are a number of perfectly rational indications for the employment of ovarian therapy in which the actual clinical results are of no especial value. In spite of the confession of

unsatisfactory results embodied in this paper, I am frank to say that I employ ovarian therapy for certain indications because I believe it to be based on rational principles, and because it is reasonable to hope that the biological chemist will sooner or later succeed in giving us ovarian extracts which will really approximate in their effects the action of the ovarian secretion intra vitam. This, after all, is the real crux of the situation as it now exists.

In conclusion, I may frankly admit that the skeptical tone of this paper reflects an attitude deliberately chosen at the outset. If there is any field of medicine in which a healthy skepticism is urgently needed, it is that of endocrinology, and more particularly that of endocrine therapy. Hyperskepticism is more to be desired than hyposkepticism, to parallel the language of the endocrinologist. The medical profession is, on this subject, now swayed by a species of mob psychology which has deprived it of its common sense and its reasoning powers.

Incalculable harm has been done by the trashy superficiality, the ignorance, and, at times, the commercialism which are reflected in much of the enormous literature which has grown up, mushroom-like, within the past decade or so. Especially unfortunate has been the influence of several books published quite recently. The author of one of these sounds his theme in the preface of his book, when he states that "only by therapy and by the use of extracts of these glands can we be led to definite conclusions." Surely he lays himself open to the charge of plagiarizing from the detail man whom we have already quoted in this paper. It is not surprising that the book in question is full of pseudo-scientific jargon. Many examples of this might be excerpted, such as this:

"If these glands which are associated with the development of the genitalia should at any period overact along these lines the child is unconsciously affected and feels a sense of attraction towards the sphere of the organs which are stimulated. This is the explanation for the slighter or greater tendency to what are called manipulations by the fingers of the organs known as the genitalia."

This book, I may add, is intended for the medical profession, and not for the public.

Or listen to this simple explanation of the menstrual phenomenon, from the pages of another recent classic:

"The amount of post pituitary secretion reaches a certain con-

centration. This in turn stimulates the thyroid and adrenal medulla. They in turn activate the ovarian cells, which congest the uterine glands and lining membrane. The follicle bursts, the ovum is discharged and wanders, the uterus waits and wonders. Nothing happens, the curtain is lowered, the scenery is removed, the actors revert to civilian clothes. That is the story of menstruation. One sees it clearly as a play of an internal secretory syndicate."

The absurdities of the purely commercial literature with which physicians of the country are being deluged, by postcard and otherwise, would be equally humorous were it not for the sad reflection that they are being swallowed by at least a fraction of the profession. It is not to be wondered at that the medical profession as a whole is showing signs of nausea, and that many formerly enthusiastic amateur endocrinologists have cast aside the whole doctrine in disgust. "Love that is too hot and strong, burneth soon away."

We must resign ourselves to the fact that future progress in endocrinology, including, of course, organotherapy, will be a slow developmental process, as it has been in all other branches of medical science. It will mean a tedious search for truth on the part of many men in many lands. Each year will add a few nuggets of knowledge, and now and then a bigger find will spur all the searchers to renewed efforts.

It cannot be said that there has been any noteworthy advance in ovarian therapy in the quarter century and more which has elapsed since its introduction. This is especially true as applied to the preparation of the commercial extracts upon which the profession as a whole is dependent.

The stellar rôle in the future development of this branch of organotherapy will unquestionably be played by the biological chemist. The time will almost surely come when we shall be able to place in the patient's circulation the specific secretions of the ovary or corpus luteum, as we now can of the thyroid, and when we shall not be obliged to strain the imagination to see good results from ovarian therapy. For the present, it would seem that this Association should function along both positive and negative lines. Not only should it endeavor to stimulate scientific thought and investigation in the field of endocrinology, but it should assume the duty of clearing from the line of advance the cluttering overgrowth of pseudo-scientific and commercial balderdash, with which it is now choked. In the words of wise old

Marcus Aurelius, let our Association "Be like the promontory against which the waves continually break, but it stands firm and tames the fury of the water around it."

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SOME RECENT WORK ON INTERNAL SECRETIONS.*

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The present day literature of endocrinology is very extensive. The bibliographic volume of the new edition of Beidl's well known monograph now runs to about five hundred pages. This includes in general only the more important contributions. Our own check list of endocrine articles for the year 1920 includes about twenty-five hundred, from nearly five hundred different periodicals, in a dozen or more languages.

Anyone with even a cursory knowledge of this literature must be impressed with the fact that it is extremely uneven in quality. A certain proportion of the articles are highly technical and of immediate interest only to the specialist. A larger proportion are articles of merely ephemeral interest, such as serve to ventilate the theories of the author or to assemble in a superficial way some of the pertinent evidence on topics of current practical interest. Between these extremes, however, is found a body of literature comprising several hundred articles a year that are of wide interest to practitioners and biologists. The difficulties confronting students in this field have been grossly under-estimated and much paper and ink have been wasted in the promulgation of immature or even fantastic literature which the actual known facts by no means justify.

Endocrinology has been in a peculiar sense an empirical field. Many of our conceptions have been obtained, not as in the case of various other fields of medical research, by induction from basic facts experimentally determined, but by observations of end results of disorders of endocrine glands, or by that most misleading of investigational methods, empirical therapeutics. There have been many attempts, however, to conform to the fashion of the times, to give a protective coloration of scientific rationalism to merely haphazard observations. I believe that much of the disapproval that has been visited upon endocrinology

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has been due to such precocious attempts at rationalizing our data when no adequate rationalization is possible.

As recently pointed out elsewhere (1), the implications of some of the common assumptions in this field have not generally been faced. The number of true endocrine organs is problematic, but many have not hesitated to postulate the existence of at least nine. Moreover, it is assumed that any one of these organs can manifest conditions of normality, dysfunction, hyperfunction, hypofunction, dysfunction plus hyperfunction, and dysfunction plus hypofunction, i. e., six different functional conditions. The possible number of distinct combinations of all these factors is 6 to the ninth power, or 10,077,696. Of these, one is normality of all glands; hence, there are, in accordance with the assumptions made, 10,077,695 possible endocrinopathies.

There are other assumptions commonly made, however, which serve further to complicate the situation. Thus, it is held that glands may function vicariously for each other, that they may stimulate each other, or that they may inhibit each other. To what extent such relationships might modify the basic combinations mentioned, imagination fails to suggest. Moreover, these combinations are presumably not static, but fluctuating. As a matter of fact, of course, the situation, even were our knowledge complete instead of fragmentary, could not be expressed by any such simple mathematics. The simultaneous operation of such variable factors could be determined only by differential calculus, and finally expressed in an inclusive formula by integral calculus (Timme). It is conceivable that our remote descendants may receive their medical and scientific information in such terms. Practically, however, our generation must be content with something very much simpler.

Such considerations serve to emphasize the complexity of the problems with which the endocrinologist is confronted and to indicate the futility of a large proportion of the superficial or imaginative out-pourings that have been accepted by an unfortunately large number as endocrine literature.

But difficult as are the problems, and slow as genuine progress has necessarily been, endocrinology has now reached a point where it must command the respectful attention of all well informed physicians. The laity are becoming versed in the

"wonders" of endocrinology. The physician must become informed as to the actual facts.

Whether or not the pineal should be regarded as an endocrine gland is questionable. It is commonly believed that a correlation between pineal tumors and somatic and sexual precocity, *i. e.*, macrogenitosomia praecox, is well established. A critical review of the literature, however, shows but few indubitable cases. It is quite possible that the peculiar manifestations of these few cases may be merely neighborhood symptoms rather than indicative of actual pineal perturbations. Perhaps the most significant contribution to the problem of recent years has been made by Dandy of Baltimore. After devising a new approach to the pineal which would involve a minimal amount of brain trauma, he found it possible to remove the gland from puppies and to keep these in apparently perfect health for months. Neither the clinical history nor the autopsy disclosed any evidence that complete extirpation of the pineal gland affected the animals in any way.

Feeding experiments have given ambiguous results. Some authors have reported stimulation of the bodily and sexual development. In a few cages of young breeding rats I noted that reproductive activity was somewhat depressed by pineal feeding. The experiments, however, have not been carried to sufficient length to be of much significance. It is quite possible that in this as in other cases the dosage factor may account for conflicting results. It is known as regards some other organ substances that results may be diametrically opposed, depending upon the amount of substance given or the attendant circumstances.

Our conception regarding the hypophysis have been somewhat unsettled recently by work in the laboratories, especially of Cushing (2) and of Camus (3) at Paris. It has been widely held that the infantilism or sex depression often seen in advanced acromegaly and other disorders due to pituitary disturbances are ascribable to functional deficiency of the posterior lobe. It has been quite convincingly shown, however, that fat dystrophy, diabetes insipidus and infantilism can be produced by relatively slight injuries of the tuber cinereum at the base of the infundibular stalk, without touching the hypophysis. This obviously suggests that the symptoms that have commonly been ascribed to

posterior lobe deficiency are due merely to disturbance of the tuber cinereum.

This conclusion is more or less supported by the fact that the true neural lobe, proper, has none of the morphological characteristics that are commonly taken to indicate secretory activity. The fact that extracts of this lobe furnish the active substance, pituitrin, is readily explainable on Herring's hypothesis that the secretions of the pars intermedia pass through the posterior lobe and infundibulum into the cerebrospinal fluid. Whether this substance is of physiologic or merely pharmacologic importance remains yet to be determined. On morphologic grounds it is probable that the physiologically active portions of the gland are those derived from the primitive pharynx, namely, the anterior lobe, the pars intermedia, the thin epithelial investment of the neural lobe proper and the recently described pars tuberalis, which extends upward along the stalk of the infundibulum.

Whether the neural lobe has any productive physiologic function or not, there is no doubt of the pharmacologic importance of its extracts, *e. g.*, pituitrin. These are widely used as smooth muscle stimulants, particularly in cases of uterine inertia in obstetrics, or in the prophylaxis and treatment of surgical shock and of intestinal atony with tympanites. The lack of toxicity of such extracts would theoretically render them preferable to ergot or eserin. Recently it has been claimed that pituitrin in repeated small doses can be used successfully to induce premature labor. Some practitioners hesitate to use the drug on account of its potency and the varying susceptibility of individual patients. It has been suggested that the danger can be eliminated by giving pituitrin on a bit of cotton held under the tongue, thus permitting control of its absorption.

The utility of pituitrin in the control of diabetes insipidus has become well established. In most cases, one to three doses of 1 cc. each per day suffice. The benefit, ordinarily, is temporary, though recovery from the disease has been reported following its use. The experience of practically all previous investigators has been that the pituitrin must be administered hypodermically. Reese and Olmstead (4), however, working at the Barnes Hospital at St. Louis, have made the interesting discovery that pos-

terior lobe extract, when given by mouth in salol-coated capsules, may control the disorder as well as do extracts given by injection.

Both in the clinic and in the laboratories a great deal of work has been done of recent years to determine the usefulness or uselessness of anterior lobe preparations. Goetsch's results from feeding pituitary substance to breeding rats have been widely quoted. It was noted that those rats which received the anterior lobe substance showed more rapid sexual development and gave birth to more offspring than did the controls. Goetsch's experiments, however, involved only a few animals and his controls were apparently not normally fertile. The subject is still under investigation in several laboratories; the general trend of the evidence seems to support Goetsch's conclusions, though numerous negative results have been obtained.

In practical therapeutics, desiccated pituitary substance is gradually gaining a recognized place. Beck of Baltimore, Englebach and Tierney of St. Louis, Timme of New York and others have obtained results in certain cases that are apparently incontrovertible. In the light of this work pituitary substance is definitely indicated in the so-called girdle obesity, the type in which fat is found predominantly in the region of the lips. In some cases, marked reduction of fat has been obtained, while in others, merely a redistribution to give a more normal body contour. In such cases, Tierney recommends that pituitary substance be used alone, at least for a period of months until it has proved either inefficacious or until the initial improvement has come to a standstill. Empirically, it has been found in the latter case that further improvement may be obtained by substituting thyroid substance. Whether the anterior lobe or the whole gland preparations are used is probably of little moment so far as girdle obesity is concerned. There is some reason to believe, however, that whole gland preparations have somewhat more extended usefulness than anterior lobe alone. Various clinicians have reported, and my own limited observations have confirmed the impression, that whole gland material not infrequently produces a striking feeling of general well-being, which seems to be correlated with increased tonicity of the muscular tissues. Observations of this sort are, of course, hard to evaluate on account of the difficulty of controlling the merely psychic aspects of the case. It should not be forgotten, however, that changes in the

subjective feelings of a patient are important realities and are by no means always psychogenic. This is sufficiently demonstrated by the conversion of a thorough going pessimist to a sunny faced optimist within an hour by an effective dose of calomel.

In case of pituitary as well as other types of organotherapy, in the present state of our knowledge, it is desirable that single gland products be used in preference to pluriglandular formulas, unless the indications for the latter are very definite. The outstanding need at the present time is to determine the independent value of each substance. One need but recall the tremendous number of theoretically possible endocrinopathies to realize the dubiety of hit-or-miss gland mixtures. Even on a basis of mathematics alone, the probability of misses greatly exceeds the probability of hits. In any unanalyzed syndrome a random gland substance is quite as likely to do harm as good. In this, as in other fields of therapy, one should remember that the primary object of the detail man or of the commercial propagandist is to sell merchandise. After all, the seductive remark, "What do you care about science, Doctor, if you get results?" is an appeal to uncritical gullibility by which many a product of little worth has been foisted upon the medical profession. If it be a legitimate argument, the profession has no ground for objecting to chiropractic, Christian science, nostrums or numerous other irregular therapeutic agencies, because all of these "get results." Any doctor should know enough about placebos to appreciate the psychology of the situation. If he does not appreciate the futility of appeals to uncontrolled "experience" he should devote a few evenings to a good history of medicine. Despite the theories of certain enthusiasts to the contrary, centuries of experience have shown that the "therapeutic test," in itself, is a most prolific source of error.

As regards the thyroid, the more important data have been widely published. That the medical profession has not adequately assimulated these data, however, is obvious from the fact that many cases of thyroid deficiency go for long periods unrecognized. Rowntree recently mentioned a case of a physician who, within the past few months, was found at the Mayo Clinic to be suffering from well marked myxedema of years' standing. He had been under the treatment of excellent practitioners, but

none of these had recognized the obvious hypothyroidism from which he was suffering. In a recent study, Anders (5) found that in 55 cases of myxedema collected from the American and Canadian literature, 74 per cent had failed of diagnosis by one or more physicians. As diagnostic signs Anders lays special stress upon the firm, inelastic thickening of the skin and subcutaneous tissue that does not pit, together with the mask-like, immobile features. The mucous membranes are often infiltrated and the teeth may become loose. The tongue, lips and nose are thick and the voice has a peculiarly monotonous character, though with frequent curious nasal explosions. Mentality is, in general, sluggish, though memory may be good. Scantiness and dryness of the hair are common. Albuminuria is frequently found. This fact often leads to a mistaken diagnosis of nephritis by those clinicians who have an exaggerated opinion of the importance of laboratory tests as contrasted with good clinical sense. In younger subjects there is one sign which, in the absence of syphilis, is practically pathognomonic,—that is, the saddle nose which results from unsymmetrical development of the craninum.

In view of the ease with which brilliant results may be obtained by thyroid therapy in these cases, it is unfortunate both for the patient and for the clinician himself when the diagnosis is missed. There is little need for laboratory tests in such cases, but basal metabolism determinations are of considerable use when the diagnosis is actually doubtful and when reliable determinations are available. Despite the usefulness of this test for orientation and control of therapy, its value is probably just now over-estimated by physicians generally. Even in border line cases the test is not conclusive of thyroid disturbances since the metabolic rate may be influenced by various factors other than thyroid perturbation. Jones (6), moreover, has recently emphasized the fact that basal metabolism determinations frequently involve a much wider margin of technical error than is commonly supposed. Several other tests for thyroid disorders are now being studied, such as complement fixation, silver reduction and quinine tolerance, but the value of each remains yet to be determined.

One important aspect of thyroid work is that of Kimball and Marine (7) on goiter prophylaxis. Evidence is accumulat-

ing that there are several distinct belts of endemic goiter in this country, one of the largest being the Great Lakes region. A careful survey was made in the Akron schools both of the incidence of goiter and of the efficacy of iodine in its prevention. It was found that only a minute quantity of iodine need be given to prevent the development of the disorder. Thus it falls within the power of the medical profession largely or entirely to eliminate a disease which, while ordinarily mild in its manifestations, has numerous serious end results, either in the patient or the offspring.

The subject of parathyroid deficiency has been studied by several recent investigators. Paton and his collaborators at Glasgow found that in experimental parathyroid tetany there appears in the urine the substance, methylguanidine. This substance was found to increase nervous irritability. Chemically, it is closely related to creatine, which, in turn, is related particularly to muscle metabolism. Hammett (8), at the Wistar Institute, studied the incidence of tetany following parathyroid extirpation in rats. The mortality in case of 102 wild Norway rats was 90 per cent. In a large number of untamed, caged albino rats the mortality was 79 per cent. When, however, parathyroid extirpation was performed on similar albino rats that were used to being handled—"gentled" animals, as Hammett calls them—the mortality was only 13 per cent. The high mortality in the excitable rats Hammett believes to be correlated with the heightened neuromuscular activity, with resulant toxin formation. These observations have an interesting bearing on the use of sedatives, particularly of calcium salts, in the treatment of parathyroid tetany. It would seem probable that the beneficial effect is due, in part at least, to depression of neuromuscular activity.

More recently, the problem has been under further study by Dragstedt and Luckhardt (9) at the University of Chicago. These investigators have emphasized the importance of the alimentary tract as a source of toxin. What is of particular practical interest is their finding that the symptoms can be controlled by measures directed solely toward decreased formation and increased elimination of toxins. By withholding animal protein from the diet and by copious administration of fluids they were able to keep their dogs alive and free from tetany for a period of

a few weeks, after which therapeutic measures could be discontinued without unfavorable results. This would seem to indicate that compensatory adjustments had taken place. It also raises the question whether the favorable results reported by a few investigators from parathyroid grafts were not due merely to such adjustments rather than to any function of the grafts themselves. The Chicago investigators regard parathyroid tetany as closely resembling other types of tetany encountered in clinical practice and point the way to more successful therapy, that is, to eliminate animal proteins and to force fluids extensively, utilizing sedatives only to the extent that is necessary to supplement these measures during the acute phase of the disorder.

As regards the thymus, little need be said. Morphologically, it lacks the characteristics of a secreting organ. It can be removed in toto from young animals with no detectible disturbance of the body function. Moreover, contrary to common impression, the thymus gland is one which is proportionately largest at birth and constantly recedes in relation to body weight until puberty, when it, with other organs, ceases to grow. In short, the thymus, in all probability, is not an endocrine gland.

Research on the adrenals continues active. Space permits only passing mention of the fact that Cannon's emergency theory has recently received support from several sources and is, in my opinion, practically established. During the past two or three years extirpation of one adrenal in the treatment of epilepsy has had considerable vogue in Germany. Some writers hold that a beneficial result has been obtained; others, that the procedure is of slight or no value. There is little in the demonstrated physiology of the glands to serve as a rational basis for the procedure and the promise of the method would not seem to be sufficient to compensate for the potential danger involved. Of more immediate practical interest is the fact that several writers have recently reported that the administration of adrenal substance is of considerable value in the treatment of exophthalmic goiter. Shapiro and Marine (10) believe that best results are obtained with fresh gland substance. In a case which they recently reported, the dosage was 5 grams daily. Larger doses caused nausea.

Perhaps the most interesting recent development in the whole endocrine field is the work of Macleod (11) and his col-

laborators at Toronto. Many investigators have dreamed of the day when the supposed internal secretion of the pancreas might be obtained in an effective form for use in the treatment of diabetes. Many experiments have been made in the attempt to obtain effective preparations, but with little success, apparently on account of the fact that the enzymes of the pancreas destroyed any hormone originally present in the pancreatic substance. The Toronto investigators made use of the well known fact that ligation of the pancreatic ducts causes destruction of the enzyme-producing cells without causing diabetes and hence, supposedly, without interference with the endocrine function. Pancreatic ligation was therefore performed on experimental animals and the atrophic gland remnants subsequently obtained and extracted. Such extracts were found to produce a considerable lowering of the hyperglycemia characteristics of diabetes. More recently, by special methods, it has been found possible to obtain effective preparations from normal pancreas material. Studies are under way to isolate the "active principle." When this is obtained it may be identified chemically and synthesized artificially, as is adrenin.

As regards the sex glands, recent work has mostly been in the hands of clinical investigators. Corner has published several important contributions on the origin and morphology of the corpus luteum, but these are chiefly of technical interest. Despite the widespread use of ovarian products in gynecology, clean-cut knowledge of their utility and of indications for their use is very slow in development. Novak (12) has recently made a careful survey of the situation and finds it desirable to recommend a distinctly conservative attitude. While brilliant results are occasionally reported in a considerable variety of conditions, many failures have also been encountered. Perhaps the greatest practical difficulty is the lack of standardization of ovarian products and, hence, of a definite base line from which to work. To those who are especially interested along this line Novak's article is commended.

As regards the male sex glands, the work of Steinach has aroused much interest together with considerable controversy, especially among German investigators. Steinach's earlier findings that sex gland transplantation may result in striking modifications of morphologic and psychologic sex manifestations has

been confirmed, particularly by Sand (13) of Denmark and Moore (14) of this country. Hence, there is excellent experimental justification for clinical studies on the efficacy of sex gland transplantation. Experimental work indicates that best results are to be expected when host and donor are closely related. The clinical studies, especially of Lydston and of Stanley, have led to promising results. Despite the sensational publicity that this work has received, the problems involved are of sufficient importance to deserve extensive study at the hands of conservative surgeons.

More recently, Steinach has turned his attention largely to so-called rejuvenation studies. He has evolved a technique of ligating the vas deferens on one side and extirpating the epididymis on the other, with the idea of bringing about atrophy of the spermatogenic tissue and stimulating the nutrition of the interstitial cells. It will be recalled that essentially this operation has had considerable vogue in the past in the treatment of prostatic hypertrophy and that rejuvenation has not commonly been seen to result. Whether, as has been suggested, this is due to the fact that sufficient care was not taken to preserve the circulation remains to be determined. Sand (15) has recently reported very striking results from carrying out the Steinach operation on a senile dog. From a lethargetic, feeble animal, the dog was converted into an active, alert individual that was able to accompany a bicycle rider in his pleasure excursions with evident signs of enjoyment.

So much for a hasty survey of a few of the results in case of the different organs. A recently introduced therapeutic procedure is worthy of brief mention, namely, that of stimulating depressed endocrine organs by light applications of x-rays. Not enough work has been done to permit any very satisfactory prophecy as to future developments, but some promising results have been reported.

Many writers have commented on the elaborate and somewhat awkward nomenclature that has developed in this field. Barker has recently proposed the adoption into English of a simple term that is gaining currency among German writers, namely, "incretion," comparable with "secretion" and "excretion." This usage would also give us the generic term, "incretory organs." The terms would seem worthy of general adoption.

In conclusion, I should like again to emphasize the fact that endocrinology, despite the world-wide interest that it has received for the past twenty years, is still in its infancy. The difficulties of investigation in the field have been greatly underestimated and many writers have given undue credence to much unreliable literature. This has led to the adoption of unfortunately extreme attitudes on the part of two groups of practitioners. The over-conservative group, who assume that the field is one merely of fantastic vagaries, overlook many substantial achievements and, somewhat wilfully, perhaps, fail to recognize that all of our knowledge of thyroid disorders and diabetes is a part of endocrinology. Their attitude, however, is more wholesome than that of the uncritical enthusiasts who assume a large body of well substantiated fundamental facts that do not exist.

It is only by careful, exacting study on the part of both practitioners and of laboratory investigators that the host of outstanding problems are to be solved. The situation calls primarily for earnest stick-to-itiveness, conservatism and whole-hearted support of proper studies upon the part both of clinicians and of experimental biologists. At the recent meetings at St. Louis the feeling was strongly in evidence that our problems are important, but that progress in their solution must be necessarily slow. Neither undue enthusiasm nor undue pessimism are conducive to the best interest of patients or of practitioners.

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CONCERNING THE PATHOGENESIS OF THYROTOXICOSIS. PART I.

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INTRODUCTION AND CONCLUSIONS

The "hyperthyroidism theory" of Graves' disease, which dates from 1884, is commonly accepted at the present time. It explains thyrotoxicosis as the antithesis of myxedema and is supported by several striking arguments. However, complete belief in this pathogenic theory has been precluded by certain conflicting data such as the frequent existence of hypo- and hyperthyroid symptoms in the same individual. During the thirty-five years since the conception of this theory, the development of our knowledge of thyroid pathology, physiology and metabolism has, especially during the past decennium, rapidly advanced, bringing to light additional facts which demand a renewed consideration of the pathogenesis of thyrotoxicosis.*

In the present article, after a brief survey of the older theories of Graves' disease, a critique of the hyperthyroidism theory is given from various viewpoints.

The facts and arguments in favor of the dysfunctional or dysthyroidism theory of thyrotoxicosis are then presented in detail. It is believed that the phenomena of Graves' disease can be most adequately accounted for on the basis of abnormal metabolic processes in the thyroid gland producing toxic effects upon the various tissues and organs, together with the systemic results due to lack of adequate amounts of the normal thyroid hormone.

More than the present knowledge of the chemo-physiology of the endocrine organs as well as of cellular metabolism is, however, necessary before we may arrive at a complete and ultimate understanding of the pathogenesis of thyrotoxicosis. Much must still be learned of the factors controlling thyroid secretion; of the intermediate steps in the synthesis of thyroxin in the human organism, of its exact chemical function and reactions in the

*In the present article the term thyrotoxicosis (Plummer) is used generically to include all local and constitutional manifestations of thyroid toxemia, including Graves' disease, so-called hyperthyroidism, toxic adenomata, etc.

repair and replacement of protoplasm as well as the exact relationship of the thyroid to other ductless glands. So many new data yet require to be obtained and duly correlated that a very conservative attitude seems indicated at present.

REVIEW OF THE THEORIES OF THYROTOXICOSIS **

The Detoxication Hypothesis. After Moebius had called attention to the predominating rôle played by the thyroid gland in the production of the symptoms of Graves' disease, Notki, followed by Blum, evolved the detoxication hypothesis. The thyroid was regarded as serving to rid the body of certain toxins. The symptoms of Graves' disease were said to develop as a result of imperfect detoxication due to a pathologic thyroid gland. With the later recognition of the internal secretion of the thyroid and the necessity of this secretion to maintain cellular nutrition growth and development, this hypothesis became untenable.

The Toxic Hypothesis. Attempts have been made to show a relationship between a chemically altered water supply and thyrotoxicosis in a manner parallel with the supposed production of endemic goiter by water of high calcium content, etc. Further study, however, showed that exophthalmic goiter is not an endemic disease and it is now known that the presence of bacterial toxins and not a changed chemical constitution in an effected water supply is necessary for the production of endemic goiter (McCarrison). The toxic hypothesis is regarded as disproven.

The Infectious Hypothesis. This hypothesis gained some headway during the period of development of bacteriology of infectious diseases, having been supported by Virchow, Kocher and others. The hyperplasia and other changes were regarded as due to direct bacterial invasion. Extended investigation demonstrated, however, that thyrotoxic as well as other goiters are sterile. Again, evidence in abundance was adduced from the surgical side showing that thyroid hyperplasia also developed as a compensatory process after partial thyrodectomy [Halsted (1) *et al.*]. The older infectious hypothesis of Graves' disease should not be confused with the modern view of the production of endemic goiter through toxemia of intestinal and probably ultimately bacterial origin (McCarrison).

**The older literature on thyrotoxicosis is given in Moebius, P. J., "Die Basedowsche Krankheit." Wien., 1906; Hölder, and Sattler, "Die Basedowsche Krankheit," Leipzig, 1909; Engelman.

The Neurogenic Theory. This theory relegates the cause of thyrotoxicosis to the central or peripheral nervous system as opposed to the "thyrogenous theory" in which the origin of the disease is regarded as being in the thyroid gland itself. Together these two theories and their modifications are the only ones receiving serious consideration at the present day.

The neurogenic theory is supported by older as well as certain new data. Charcot, Marie, Gauthier, Trousseau, Gerhardt, *et al.*, regarded exophthalmic goiter as a disease of the entire nervous system, calling especial attention to the symptoms and signs of increased central, peripheral and vasomotor stimulation present.

This theory then developed in two divergent ways, one school emphasizing lesions in the central nervous system, particularly the medulla; the other, in the autonomic.

The Bulbar Theory was ably supported by Sattler, an unusually thorough student of Graves' disease. Sattler inferred from the frequency with which the cardinal symptoms, goiter and exophthalmos, were associated, that pathologic processes in the medulla or in still higher portions of the central nervous system must be present. The well known experiments of Filehne (2), corroborated by others, showed that on sections of the *corpora restiformes* of rabbits, exophthalmos, thyroid hyperemia and tachycardia occurred. Unilateral bulbar lesions produced such symptoms on one side only. Sattler also calls attention to the cranial nerve palsies, which sometimes are met with in Graves' disease; also the glycosuria and speech defects, as possible bulbar symptoms. The muscular spasms, contractures and paralyses can also be accounted for by the bulbar hypothesis (von Leube).

Other adherents to the neurogenic theory regarded the *peripheral* nervous system, particularly lesions and degenerated areas in the cervical sympathetic ganglia, as responsible for the disease. Thus, lesions in the upper cervical ganglion would effect motor and secretory cells in the muscle of Mueller, the thyroid and heart; in the median ganglion, the thyroid and heart; in the inferior, the heart alone. Eppinger, Falta, Rudinger (3) and Eppinger and Hess (4) have supplied many experimental and theoretical data in support of this view. Its most enthusiastic adherents maintain that Graves' disease with fully

developed sympathicotonic symptoms is necessarily due to the above origin.

Support of this viewpoint from the pathologic side has been supplied by L. B. Wilson (5), who showed that experimentally produced lesions in the cervical sympathetic ganglia may cause histologic changes in the thyroid paralleling those found in the exophthalmic goiter. Wilson concludes that the thyroid is stimulated to abnormal function usually as a result of local infection in the cervical sympathetic ganglia. Cannon and Cattell (6) have also recently demonstrated the activation of the thyroid to secretion by the sympathetics.

Criticisms of the Neurogenic Theory. The neurogenic theory properly emphasizes the importance of the nervous system in the pathogenesis of thyrotoxicosis. It has, however, proven inadequate to withstand various criticisms which will now be mentioned.

From the clinical standpoint, the presence of an irritative ganglionic lesion is usually assumed to account for the exophthalmos (contraction of the Muellerian muscle) and tachycardia (stimulation of the cardio-accelerator fibers). But how account for the thyroidal hyperemia and hyperplasia, which are best explained by a paralysis of the vasomotor fibers and a direct metabolic stimulation from the blood stream (example, increase in the goiter and clinical symptoms due to iodine administration)? The absence of pupillary contraction and presence of dilatation which actually occur in exophthalmic goiter would make it necessary to accept a selective stimulation of certain autonomic fibers and paralysis of others, which is paradoxical and does not merit credence. Murray pertinently remarks that irritative cervical sympathetic lesions in order to account for the symptoms must necessarily be regarded as persisting for many years in most cases, which is inconsistent with the usual reactions of neuroganglionic tissue to pathological stimuli. Filehne's rabbit experiments, in which certain symptoms of Graves' disease were produced, have also been criticised by Marie, who declares that such are no more Graves' disease than is the glycosuria produced by bulbar puncture to be regarded as true diabetes mellitus. [See C. P. Howard's (7) excellent critique of the Neurogenic Theory.]

Pottenger (8), a close student of visceral neurology, has recently emphasized that many thyrotoxic symptoms are actually

parasympathetic in origin, viz.: Von Gräfe's sign, Dalrymple's sign, epiphora, sudorrhea, diarrhoea, hyperacidity and eosinophilia. The neurasthenia, change of psyche, and tremor are to be regarded as of central origin. The nervous stimulation is, therefore, considered a general one involving in varying intensity the several portions of the nervous system, central, peripheral and vegetative, and consequently not confined to the sympathetic ganglia.

We have, furthermore, direct clinical evidence that *thyrotoxicosis can arise without primary involvment of the nervous system,* in those cases in which the disease has developed as a direct sequela of acute thyroditis or as result of trauma to the thyroid.

From the pathological side there is also serious objection to a purely neurogenic theory. Many careful autopsies on patients dying of exophthalmic goiter have failed to demonstrate the regular occurrence of lesions in either the medulla or the cervical sympathetic ganglia. Again, bulbar disease with demonstrable pathologic changes is not found associated with the symptomatology of thyrotoxicosis more often than can be regarded as mere coincidence, although, according to the bulbar hypothesis, the reverse should be true.

The chief question in point, it would seem to me, is whether Graves' disease arises endogenously in the thyroid gland itself or from neurogenic cause. An *exclusively* nervous origin of the disease is untenable as it has been demonstrated in many thousands of cases that the surgical removal of the major part of the thyroid gland is usually followed by subsidence of the signs and symptoms. From this general experience, the deduction is irrefutable that whatever indirect influence the nervous system may have in the production of the disease, the same evidently originates as a result of pathological changes in the thyroid itself. Persistence of the symptoms after thyroidectomy can be explained by pathologic and metabolic changes in the portion of the thyroid remaining after operation, together with permanent lesions in various organs due to previous effects of the thyrotoxic condition.

On the other hand, it is impossible to deny the marked influence of the nervous system, especially in those cases of thyrotoxicosis developing suddenly after fright and various other forms of mental shock. Cannon's recent demonstration of the

influence of psychic states and adrenalin upon the secretion of the thyroid secretion emphasizes the intimate relationship of the thyroid to the nervous and endocrine systems.

In résumé, then, of the value of a purely neurogenic theory of thyrotoxicosis this theory may be dismissed as untenable in view of present evidence without, however, recognizing that the fundamental metabolic disturbance in the thyroid gland in this disease may be set up and largely influenced by psychic, trophic and endocrine factors under nervous control; also that toxic products of thyroid metabolism selectively attack nervous tissue.

Crile's (9) *Kinetic Hypothesis* may be briefly mentioned in connection with the neurogenic theory. This distinguished surgeon endeavors to correlate the nervous symptoms and lesions with those of the thyroid gland by regarding the disease as one affecting "the motor mechanism of man, the same mechanism that causes physical action and that expresses the emotions." "A pathological reaction" between the brain and the thyroid is produced by various nervous factors causing the disease to develop. The arguments advanced in favor of this rather nebulous hypothesis are not capable of exact critical analysis.

THYROGENIC THEORY

The Hyperthyroidism Theory of Thyrotoxicosis. If then a purely neurogenic origin of the disease is discarded, the cause must be sought in the thyroid gland itself. The *thyrogenic theory* is capable of two chief conceptions, the "hyperthyroidism theory" which ascribes Graves' disease to hyperfunctional condition of the thyroid as opposed to a "dysfunctional" or "dysthyroidism" state in which the secretion of the gland is regarded as qualitatively altered. At present we are concerned with the pure "hyperthyroidism theory."

This view was first promulgated in 1884 by Rehn (10), although it is generally first ascribed to Moebius (11) (1886), who, however, while emphasizing the importance of the thyroid in the causation of exophthalmic goiter regarded the disease as due to increased but qualitatively altered thyroid secretion. Eminent students of the disease soon accepted this standpoint in principle, although from the first many have adhered to the dysfunctional theory. Among those who have supported the hyperthyroidism theory are Kocher, Reverdin, Gauthier, F. Kraus, Falta, L. B. Wilson, Plummer.

The chief data supporting the hyperthyroidism theory are the following:

1. The thyroid tumor and histological evidence of hyperplasia.
2. Relief or cure of the disease by thyroidectomy.
3. Experimental production of hyperthyroidism in man and animals by thyroid medication.
4. Increase of symptoms of thyrotoxicosis on exhibition of thyroid preparations.
5. The contrast shown by the symptoms and signs of "hyperthyroidism" and hypothyroidism (Kocher) as well as by the metabolism.

The hyperthyroidism theory is therefore apparently based upon some of the best known facts pertinent to thyrotoxicosis. The clear explanation of the morbid picture afforded by this pathogenic conception has greatly aided its general acceptance up to the present time. As so frequently experienced in the difficult science of medicine, a definite explanation of otherwise a peculiarly confused clinical picture is so attractive that even an array of other facts irreconcilable with such a simple theory are often overlooked or disregarded by most physicians. The inadequacy of the hyperthyroid theory to account for present knowledge of thyrotoxicosis can best be shown by criticising *ad seriatum* the above mentioned arguments supporting this etiologic hypothesis, prefixing such criticism with important *a priori* grounds for questioning the same.

CRITICISMS OF THE HYPERTHYROIDISM THEORY

Criticisms on a priori grounds. If viewed from a broad physiological viewpoint, it is questionable whether the conception of "hyperfunction" has a sound basis, however convenient and ingenious it may be. We may seek through the whole realm of organology without finding a single instance of an idiopathic hyperfunctional condition such as is claimed for the thyroid in Graves' disease. Hypertrophy, hyperplasia and hyperfunction only ensue under normal conditions when there is a cause and demand for such a reaction either by additional functional strain on a normal organ or through depression of normal function through disease. For example, the heart of the mountaineer hypertrophies and increases its power through circulatory

stimuli produced by the higher altitudes. Again, cardiac hypertrophy results from hypofunction due to toxic degeneration of the myocardium. Acromegaly might be advanced as an exception to this rule, but even here the excessive overgrowth is asymmetrical and abnormally confined to the jaws, hands, feet, etc. It is accompanied by decreased physical and psychic vigor and general degenerative processes. This antithesis is so marked that the most eminent students of pituitary disease, including Cushing, do not accept a "hyperfunctional" condition of the hypophysis. Indeed, it is very questionable whether the general credence given to the conception of hyperfunction as applied to various endocrine diseases or symptom complexes, including exophthalmic goiter, is justified by present knowledge. There are many more current beliefs in modern clinical medicine which are generally held without scientific foundation or substantiation.

The function of the thyroid gland is largely one of control of growth and development. In cretinism both are markedly deficient. If, then, we unreservedly accept the "hyperthyroidism theory" of Graves' disease, we must regard the thyroid in this condition to be in a state of continual hyperfunction. If cretinism is the antithesis of Graves' disease, then we must needs expect a state of over-growth and over-development to be found in young thyrotoxic subjects, while actually there is no true over-growth and at times slight signs of retarded development. The elongated limb bones observed in cases of youths suffering from Graves' disease have been erroneously regarded as evidence of over-growth, whereas this phenomenon is actually due to the delayed sexual maturity (failure of gonodal stimulation of closure of the epiphyses).

Pathological Evidence. The presence of hypertrophy of the thyroid gland in thyrotoxicosis has been used as one of the chief arguments for accepting an overfunction or overproduction of thyroxin as the cause of this disease. According to this view, the degree of hypertrophy present should be found to vary directly with the severity of the clinical symptoms. This, however, does not hold true. Some large goiters are accompanied by slight symptoms and conversely a very small goiter may be present in a very severe case of Graves' disease. Certain individuals show even marked symptoms without demonstrable thyroid hypertrophy.

Exophthalmic goiter is believed to follow great nervous and physical exhaustion or shock. It also occurs during or as a sequela to acute thyroditis of bacterial origin, also various acute infectious fevers. In these exhaustive and depressant conditions, it is paradoxical to accept etiologically a hyperfunctioning organ which would actually demand unusually good, not poor, nutrition. In particular, it seems to the writer that the development of thyrotoxic symptoms in the course of an acute thyroditis demands for their explanation, the recognition of morbid metabolic processes due to actual pathologic lesions in the secreting tissue, which a hyper-secretory hypothesis could but lamely explain.

Reasoning logically, one should expect marked hyperplasia of the thyroid to be regularly accompanied by the symptoms of thyrotoxicosis and conversely thyrotoxicosis to be as routinely associated with hyperplasia. In testing this assumption, we may refer to the most extensive and accurate pathological researches on goiter of the Mayo Clinic. According to Wilson's (12) and Plummer's (13) careful studies nearly all thyroidectomized patients had hyperplastic thyroids, but hyperplasia evidently does not necessarily lead to exophthalmic goiter, for of the non-hyperplastic goiters removed, 23.3 per cent were from patients showing thyrotoxic symptoms. Plummer (14) has, of late, remarked, "Areas of hypertrophy, 'some hypertrophy' (MacCarty), are present in such a percentage of all thyroids resected that this degree of hypertrophy has little, if any, tangible significance. In exophthalmic goiter, diffuse hypertrophy of the thyroid is rarely absent, but even in severe cases it varies from the most marked degree to the vanishing point." According to Boothby's (15) recent statistical report of 1,656 cases of goiter with histological studies, 254 were classified as non-toxic adenomata, i. e., as hyperplastic goiters without toxic symptoms, and 366 as toxic adenomata accompanied by thyrotoxic symptoms. Boothby states, "The pathologist, however, cannot distinguish adenomas which produce hyperthyroidism from those which do not." It is also shown from the numerous cases of this clinic that at least 16 years elapse from the development of adenoma to that of the appearance of thyrotoxic symptoms in the same individual. Marine and Lenhart (16) have also shown that there is no constant relationship between the degree of hyper-

plasia and the cardinal symptoms, exophthalmos and tachycardia. These authors also emphasize that hyperplasia is very common in simple goiters and other types of thyroid disease in which thyrotoxic symptoms are absent.

It follows from these amply demonstrated facts that the presence of thyroid hypertrophy and hyperplasia can have no direct etiologic bearing on the production of thyrotoxicosis, for hypertrophy and hyperplasia may be present without the development of thyrotoxicosis; the reverse may also be true.

Surgical Evidence. A chief argument for the acceptance of the hyperthyroidism theory has been the fact that surgical removal of the major part of the hyperplastic thyroid gland usually leads to cessation of the symptoms. This argument loses its apparent conviction, now that it has been shown that thyroid hypertrophy and hyperplasia cannot *per se* be responsible for the disease. Another explanation must be found for the hyperplastic processes in various thyroid diseases, including thyrotoxicosis (See below).

The surgical cure of the disease has indeed nicely demonstrated that the toxic excitant of the morbid process has its origin in the gland itself, but brings no proof that the varying degree of hypertrophy and hyperplasia is the cause of the disease. Surgical experience has, on the contrary, made it clear that the pathogenic processes do not necessarily depend upon the presence of an intact, hyperplastic and supposedly hyperfunctional gland, for in certain obstinate cases the symptoms may not subside so long as the tiniest rest of the toxic gland is allowed to remain. This not uncommon observation is excellent evidence that an intensive metabolic disturbance in the thyroid is at fault rather than a simple hyperfunction which would necessitate the presence of a large mass of thyroid tissue in order to produce the disease.

Clinical Evidence: The relation of the iodine content to the degree of hyperplasia is of interest in this regard. As iodine is organically combined in the thyroxin molecule the amount of iodine present in the gland can be properly considered a certain gauge of its metabolic activity, duly recognizing, however, that such determinations cannot comprehend the amounts of iodine secreted in molecular association in thyroxin. It has been found that hypofunctioning goiters accompanied by cretinism are

markedly deficient in the iodine content. According to the hyperthyroidism theory one may then expect to find more rather than less iodine in thyrotoxic thyroids. Actually, Kocher (17) has noted as little as 1/30 of the normal amount present; Wilson and Kendall (18) from 1/50 to 1/20 of the normal. According to Marine and Lenhart's (19) studies, the iodine content of exophthalmic goiters varies inversely with the amount of hyperplasia present and shows in this regard no departure from the behaviour of the iodine content in various other thyroid conditions, normal and abnormal. Thus hyperplasia is known to decrease in non-toxic thyroid adenomata on exhibition of iodine or thyroid substance and iodine is stored in the gland. Precisely the same behaviour was observed by Kocher and Marine and Lenhart on administration of iodine and thyroid preparations to exophthalmic goiter patients. From these observations, it is evident that no evidence from the behaviour of the iodine content in exophthalmic goiter can be adduced in favor of the hyperthyroid theory.

Experimental "Hyperthyroidism": The similarity of the symptoms following the ingestion of thyroid material in excess of that of Graves' disease, also the well known aggravation of the disease by thyroid medication, constitute a further support of the hyperthyroidism theory. These statements are substantiated by experimental and clinical data which will now be analyzed.

From the experimental side, Klose (19) and Lampe, Liesegang and Klose (20) have reported the production of exophthalmic goiter symptoms, i. e., elevation of temperature, tachycardia, glycosuria, increased nervous irritability and, rarely, exophthalmos by feeding exophthalmic extracts to certain strains of fox terriers. These are among the very few experiments known to the writer in which exophthalmos, a cardinal symptom of human Graves' disease has been produced. Ballet and Enriquez (21), Baruch (22) and Kraus and Friedenthal (23) likewise report the production of exophthalmos by feeding thyroid preparations. Such results, however, merely demonstrate that extracts from the *pathological* thyroids of Graves' disease patients can produce a similar condition in animals, but do not prove that Graves' disease can be produced in animals by feeding large amounts of thyroid tissue or the thyroid hormone, which must be demon-

strated to prove the hyperthyroid hypothesis. Klose and his associates, however, failed to elicit the above symptomatology when extracts from normal thyroid glands were fed and they themselves interpreted their results as supporting the dysthyroidism theory.

A large number of workers have administered various iodine and thyroid extracts; also divers preparations from normal, goitrous, or thyrotoxic individuals without the appearance of a clinical syndrome capable of being designated as exophthalmic goiters. Among these may be mentioned Cunningham (24), Soupault (25), Hutchison (26), Gley and Claret (27), Gley (28) (who repeated Klose's work), Schoenborn (29), Fonio (30), Carlson, Rooks and McKie (31), Marine and Williams (32). Kendall (33) in injecting goats and dogs with large amounts of the isolated thyroid hormone gave the hyperthyroidism theory a severe test, but failed to observe the development of Graves' disease. This author states, "The general picture could not be differentiated from parathyroid tetany, idiopathic tetany or from certain phases of epilepsy." Though tachycardia and hyperpyrexia were produced, no exophthalmos was noted.

Summarizing then these data on the experimental causation of Graves' disease in animals, one must admit that the weight of evidence is against acceptance of the reproduction of this disease experimentally through use of thyroid preparations, including the thyroid hormone in chemically pure form.

DISCUSSION OF THE CLINICAL EVIDENCE IN FAVOR OF THE HYPERTHYROIDISM THEORY

From this side is reported the well known case of Notthaft (34) whose patient ingested 1,000 thyroid gland tablets within 5 weeks. There followed the development of the complete picture of exophthalmic goiter which gradually subsided when the thyroid medication was stopped. Several other similar cases have occurred in the literature. The writer has learned of still another by verbal communication of Professor Graham Lusk, New York.

It is, however, remarkable that, although over-dosage with thyroid preparations is of not uncommon occurrence, the number of such cases has remained extremely few. These rare instances in which toxicity does occur, it would appear, might be accounted for by the previous existence of a latent tendency to

thyrotoxicosis, which, on the stimulation by the thyroid preparations, thereupon developed. Proof of the hyperthyroidism theory by such means would also necessitate the demonstration of an unquestionably normal thyroid gland in such instances. This is lacking and impracticable as well. It is also a well established clinical fact that most cases of exophthalmic goiter develop severer symptoms after the exhibition of thyroid preparations [Cerioli (35), Kocher (36), Goldflam (37), *et al.*]. This aggravation of Graves' disease by thyroid medication can, however, only superficially be regarded as supporting the hyperthyroidism theory, for it is susceptible of other explanation. Thus the ingestion of large amounts of iodine and thyroxin may merely serve to provide a dysfunctioning gland with added material for the production of a toxic, imperfectly synthetized or anabolized thyroxin molecule, which may be the ultimate cause of the disease.

Finally, all experiments known to the writer on the experimental or clinical production of Graves' disease by thyroid preparations are subject to the same criticism; the question as to their interference with the normal thyroid metabolism with possible production of aberrent or pathological metabolites in the thyroid, which, themselves, cause the toxic symptoms. Convincing proof of the hyperthyroidism theory can only be brought by first excising the thyroid gland in experimental subjects and then producing *all* symptoms of the disease by introduction of large quantities of normal thyroid gland or, better, thyroxin. Such proof for the hyperthyroidism theory has not been forthcoming. One is here reminded of the inconsistency shown by the ready acceptance by many physicians of the experimental production of Graves' disease in animals on quite insufficient evidence, whereas the bacteriologist refuses to accept the bacterial cause of a given disease without its exact reproduction in animals or man.

The Contrast shown by the Symptoms and Signs of "Hyperthyroidism" and Hypothyroidism has been advanced in most text-books as a proof of the hyperthyroidism theory ever since the great emphasis put upon this apposition by Kocher. In regard to the value of the general clinical antithesis of these two conditions, McCarrison has shrewdly observed that the contrast shown by their symptomatology brings us no nearer the eluci-

dation of the *cause* of the morbid state of either. It seems to the present writer that it would be just as illogical to argue that acute mania is caused by "hyperfunction" of the higher cerebral centers because this form of insanity shows a diametric opposition, clinically, to acute melancholia. Such an argument would be regarded by every one as purely speculative.

Considered purely clinically, exophthalmic goiter presents a general picture of stimulation of the entire nervous system, a number of symptoms, viz., increased excretion of nitrogen and elevation of metabolism, the vagotonia, hyperpyrexia, nervous excitability, etc., differing only in degree from well known reactions of the organism to bacterial toxins, etc. On the other hand, the clinical picture of myxedema is one of widespread degeneration and consequent loss of function due to the loss of the anabolic action of the thyroxin on the tissues. The contrasting symptomatology of these two diseases is therefore most reasonably explained by a chemo-toxic effect in Graves' disease and loss of function in myxedema and cretinism, two essentially different pathological conditions producing, of course, differing symptoms.

Furthermore, a critical survey of the *complete* symptomatology of both diseases renders it evident that the clinical antithesis of Graves' disease and hypothyroidism is largely confined to certain prominent symptoms as shown by the contrasting facial expression, mentality, the pulse rate and the like. In fact, a number of identical symptoms and metabolic phenomena are present in both conditions. Even Kocher admitted the common presence of edema, dryness and loss of hair and hair color, cutaneous dryness and pigmentation, and diminution of the salivary secretion. In addition to these, there are other trophic and nutritional disturbances occurring in the two diseases but cloaked in the case of Graves' disease by the more striking evidences of general nervous excitation. To avoid repetition, reference can be made to the detailed consideration of the symptomatology from this standpoint developed in a later section.

Aside, however, from the identity of a number of the symptoms, a chief argument against acceptance of the hyperthyroidism theory has always remained the constant occurrence of a number of cases where clinically myxedema has been found accompanying Graves' disease. It is impossible to account for this condition on the hyperthyroid hypothesis. As Faure has em-

phasized, the conception of a thyroid gland in coincident state of hyper- and hypo-function is paradoxical. This fact alone would seem to the writer effectually to militate against the acceptance of the pure hyperfunctional theory.

Furthermore, myxedema is occasionally met with as a sequela of Graves' disease. Here may also be mentioned the not uncommon familial occurrence of Graves' disease and exophthalmic goiter. These facts would argue a common, not a diametrically opposite, etiology.

Metabolism in Graves' disease and the Hyperthyroidism Theory. The increased metabolism in Graves' disease and the decreased metabolism in hypothyroidism is another argument used in favor of the hyperthyroidism theory. In order to apply certain criticisms to this argument it is necessary to analyze known metabolic data in thyroid disease.

During the past few years, since the general introduction of basal metabolic rate determinations in the study of thyroid disease, the contrast of thyrotoxicosis and myxedema has been further emphasized by the marked differences in the height of the gaseous metabolism in these two conditions. This metabolic antithesis has been particularly brought out by Plummer and Boothby, *et al,* of the Mayo Clinic in numerous articles which have served, on account of the large number of such metabolic studies reported and the prominence of their source further to strengthen the case of the "hyperthyroidism theory" among the medical profession at large.

The great assistance afforded the clinician by metabolic rate determinations in the diagnosis and treatment of thyroid disease has, however, led to overestimation of the importance of basal metabolism determinations in the diagnosis of these conditions. The influence of the thyroid as a regulator of oxygen consumption and of energy production has thus been thrust into the foreground without due consideration of the importance of thyroid function in cellular nutrition. Exception is here taken to the definition of the thyroid hormone advanced by Plummer and Boothby (38), influenced by Kendall's chemical viewpoint. They regard thyroxin as "a catalyst that accelerates the rate of formation of a quantum of potential energy in the cells of the organism." It is questionable whether this definition can be regarded at present as more than purely speculative, inasmuch as we re-

main in considerable ignorance of the exact chemical reactions involved in the formation of the "potential energy" in question. The frequent quotation, however, of this hypothesis in recent publications seems sufficient proof of the seriousness with which it has been generally received by the medical profession at large. This is due to the prominence of the source of this view. It would likewise indicate the desirability of authoritatively advancing only such new theoretical viewpoints as are completely defensible, both by critical analysis of the pertinent literature and adequate experimental support.

The chief function of the thyroid gland is the regeneration of old and growth of new cells by aiding in the synthesis of protoplasm. An attempt at a more specific definition seems inadvisable at present. This *anabolic* function is of vastly more importance than its catabolic effect, i. e., the production of heat and energy through combustive processes requiring oxygen. Both anabolism and catabolism, however, require oxygen consumption with liberation of heat, energy and carbon-dioxide. *The metabolic rate is very probably influenced by the thyroid, not directly for the purpose of control of energy and heat production, but only to the extent that these processes are necessary in the chemical reactions leading to the accumulation of intermediary metabolites and their synthesis into old or new protoplasm by the aid of the thyroid hormone.*

This view of thyroid function, which should indeed be self-evident from the marked influence that the thyroid is known to exert upon growth, was first emphasized by the present writer (39) in 1916, and developed in a later paper (40).

Even athyroid individuals are capable of considerable release of energy and heat production through other agencies, probably other ductless glands, which also function in the general nutritive processes of the cells. In cretinism and myxedema, even when there is complete absence of the thyroid gland, the gaseous exchange is decreased at most to 40 or 50 per cent, so at least 50 to 60 per cent of the normal metabolism must be accounted for otherwise than by activity of the thyroid gland. It will also be remembered that the heat centers in the medulla are still functioning even in athyreosis, as evinced by their response with pyrexia when sufficiently stimulated by bacterial toxins.

It is indeed probable that the decrease in the basal metabolism in hypothyroidism is to some extent *a compensatory retardation of the chemical processes of the cells of the body, whose exhaustion and disappearance would be hastened, in absence of a normal thyroid, by normal metabolic processes.* This seems indeed probable by the observed drop in the metabolic rate in cases of inanition with intact thyroids to levels as low as those seen in severe cases of cretinism and myxedema. That the lowered metabolism in hypothyroidism is due at least in part to "hormone starvation" is suggested by the gradual fall of the basal metabolism after complete removal of the thyroid, though it is capable of other explanation.

In view, then, of this conception of the metabolism of hypothyroidism, the decrease of the basal metabolic rate in hypothyroidism is regarded as a measure of an accompanying metabolic phenomenon rather than indicative of failure of a fundamental thyroid function.

The conception of the increased metabolism in thyrotoxicosis as being due simply to increased energy production, through increased thyroxin production, *i. e.*, "hyperfunction" and "hyperthyroidism," is likewise subject to considerable criticism. Although a general indication of the severity of the disease, it has not proved possible to demonstrate an exact parallelism between the amount of "hyperfunctioning," thyroid parenchyma and the degree of elevation of the metabolic rate. Every internist of experience has observed cases of thyrotoxicosis still presenting considerably increased metabolic rates (for example, an increase of even 50 per cent) in individuals who possess but one-tenth or less of a toxic goiter largely removed through operation. Indeed, it is far more logical to explain the elevated metabolism in Graves' disease as a result of a general intoxication from abnormal products of thyroid activity. This reaction differs chiefly in degree from that produced by bacterial and other toxins in fevers, as has been stated. With regard to the increase in the metabolic rate observed after administration of large amounts of pure thyroxin, this observation fails to bring proof that the augmented gaseous exchange is not likewise due to a toxic stimulation, from the development of toxic intermediate products in course of the catabolism of amounts of thyroid hormone introduced experimentally in excess of requirements.

It by no means necessarily follows that the results ensuing after an ingestion of abnormal amounts of thyroid substance influence the basal metabolism *by the same means* in which it is held to the normal level by a normally functioning thyroid. Indeed, the very presence of a number of peculiar nervous and other symptoms in experimental hyperthyroidism would suggest a probable change in composition of the thyroid hormone responsible for the same. The long latent period reported by Kendall (41), as well as Janney and Isaacson (42) following the administration of a toxic dose of thyroxin can be considered as evidence in favor of some chemical transformation being necessary *before* the toxic outbreak with elevation of the metabolic rate can take place. Otherwise, one would expect an *immediate* rise of the basal metabolic rate which under normal conditions is one of the most labile of natural phenomena.

The Protein Metabolism. The known facts concerning other aspects of the metabolism of hypothyroidism as contrasted with Graves' disease do not bear out the suggestion made by the behavior of the gaseous exchange, namely, that the one process is antipodal to the other,—"hypofunction" versus "hyperfunction." Although the nitrogen metabolism is generally decreased in the former and increased in the latter condition, still the writer's experiments (40) have made it probable that the decrease of nitrogen output in cretinism is due rather to decreased protein absorption secondary to a decreased ability to retain synthetically nitrogenous metabolites in the body; possibly also to nitrogen "sparing." In thyrotoxicosis the increased nitrogen output is best explained as a toxic loss of protein and nitrogen. It may also be noted that Janney (40), as well as Halvarsen, Bergeim and Hawk (43), found it possible to obtain an increased nitrogen balance by administering thyroxin to Graves' disease patients, a procedure which, according to the hyperthyroidism theory, should always have the opposite effect.

Creatinuria is frequently present in both Graves' disease and myxedema. Although *hyperglycemia* is the rule in the former and *hypoglycemia* in the latter condition, there is little regularity in this. Speaking generally, the most we can state is that irregularity in the carbohydrate metabolism is present in both diseases. In view of these discrepancies, it is impossible longer to accept that contrast shown by the metabolism of thyro-

toxicosis and hypothyroidism is conclusive evidence of the validity of the hyperthyroidism theory.

Summarizing then the foregoing data, criticising the value of the contrasting behavior of the metabolism in hypothyroidism and thyrotoxicosis as a support of the hyperthyroidism theory, the following may be said.

1. As the chief function of the thyroid is the generation and regeneration of the tissues by action of thyroxin on protein metabolites, not that of a mere catalyzer for the combustive processes, the basal metabolism, however significant clinically, is not of fundamental importance in the theory of thyroid disease.

2. The lowered basal metabolism of hypothyroidism and the elevated metabolism of thyrotoxicosis are subject to other explanation than that of increased or decreased heat and energy production due to a simple kinetic hypothesis. The lowered metabolism of hypothyroidism may be caused at least in part by a compensatory retardation of metabolic processes in the cells to offset the decrease in amount of thyroxin, a hormone necessary for growth and repair of the cells and tissues. The increased gaseous exchange in thyrotoxicosis can be more reasonably explained by a toxic stimulation of the nervous and other tissues than by the effects of simple over-accumulation of the normally non-toxic synthetic hormone, thyroxin.

3. The characteristics shown by protein, creatin and carbohydrate metabolism in exophthalmic goiter and hypothyroidism are not such as can be satisfactorily explained by the hyperthyroidism hypothesis.

Summary of Criticisms of the Hyperthyroid Theory: In the preceding pages the chief data and arguments in favor of the "hyperthyroidism theory" have been analyzed and reviewed in the light of modern knowledge. Sufficient evidence, it is believed, has been advanced to show that this time honored theory is supported by superficial and, in part, conflicting arguments, which constitute but a fallacious explanation of the etiologic, pathologic, metabolic and clinical data of Graves' disease.

(To be continued)

EXPERIENCES IN TESTICLE TRANSPLANTATION

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NEW YORK

I believe these cases are more often referred to the plastic surgeon than to the general or genito-urinary operators.

The writer has had three cases referred to him during the past twelve months. That insufficient time since operation has elapsed, in the two which were operated on, is not questioned, as far as feeling in a position to state a definite result. I am reporting the cases, stating facts, as they were before operation and as they are now. I make no prognoses.

The first case, Mr. E. W. K., aged sixty, following a sudden mental shock in 1919, became completely impotent for a period of three months. He recovered to such an extent that he was able to get a partial erection after the administration of strychnine and a glandular extract. This period of ability to have a partial erection lasted until March, 1920, when he suffered a second mental shock to be followed again by the return of complete impotence. This second attack of impotence was associated with considerable debility, weakness in the lower extremities and insomnia. Glandular extracts and aphrodiziacs produced no beneficial result.

On June 29th, 1921, through the courtesy of the laboratories of Armour and Company, I secured a fresh testicle of a ram sent to my office in a refrigerated state. I refrigerated this gland in boric acid solution for thirty hours more and then making a longitudinal section 1 cm. in thickness, transplanted it into the patient's abdominal wall. The course of events in this case were as follows: Two days after operation the patient stated that he had enjoyed the first perfect night's sleep he had had in seven months and on awakening felt refreshed from his sleep, something he had not done before his insomnia began. Seven days afterward the center of the transplanted tissue began to become necrotic and an exudate began. Nine days after the patient began to have erections in the mornings. By the twentieth day the entire center of the transplanted gland had sloughed away, the wound had closed and the periphery of the gland could be

distinctly felt. Normal sexual life, an increased appetite and a general feeling of well being now ensued. The patient attributed all his general improvement to the operation. At the end of six months he reported a gain of fifteen pounds in weight. Last month (May, 1922) the patient called to request a reduction of his bill on the ground that he had changed his mind about the benefits received from the operation . . . that since receiving the bill and thinking matters over he felt that his entire improvement or at least the greater part of it was psychological . . . so there you are!

The second case, J. P. R., referred to me by Doctor F. Mitchell of Sailors' Snug Harbour Hospital, Staten Island, N. Y., gave the following history: Age 65; white; occupation, retired infirm sailor; state, bachelor. For seven years had been suffering with the general symptoms of debility. For the previous six months he had required assistance in ambulating, using two canes or a cane and crutch. He had been unable to have copulation for months (six) due to lack of erections. Weight, 140 pounds.

Through the courtesy of the same laboratory, I secured a testicle of a freshly killed ram and within the hour transplanted a section similar to that used in case No. 1, using the same general technic except the refrigeration. The reaction was marked. Within forty hours the patient was confined to his bed, the abdomen was swollen and tympanitic, the temperature and pulse rose and the patient was genuinely sick. Sloughing began on the seventh day and lasted three weeks. At the end of this time he had recovered sufficiently to come to my office. He had discarded his canes or crutch and cane. (The operation was performed October 13th, 1921; his visit to my office, Nov. 8th, 1921.) I have seen this patient many times since operation. In January his hair, which had been gray, began to become brown and at the present time he shows but a scattering of gray hair. He states that he awakens daily with an erection and can copulate at will. Very little of the original gland can be palpated. This patient's general appearance, movements and cerebration have so markedly improved that it seems that only a biased mentality could think of denying the beneficial effects of the testicular gland.

The third case mentioned, referred by Drs. Williams and

Becket of the same institution in which case No. 2 was a patient, is a man of 48 years of age who became blind and impotent simultaneously while in Government service in the Philippines ten years ago. This case is so recent (having been operated on only during the present month) that it is of no clinical interest at present and only mentioned on account of the peculiar coincident blindness and impotence.

Addendum—Aug. 15, 1922. Potency was recovered in this case three weeks following operation.

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Book Reviews

THE ORGANS OF INTERNAL SECRETION, THEIR DISEASES AND THERAPEUTIC APPLICATION. Ivo Geikie Cobb, M.D., M.R.C.S. 3 ed. New York, 1921. Wm. Wood & Company. 352 p.

A review of a previous edition of this work was published in this journal, 1917, **1**, 469. The present edition does not vary greatly from that previously reviewed. As indicated in the title, the book is an attempt to place at the easy disposal of clinicians those data of endocrinology that are of direct practical use. An attempt is made to rationalize the data presented by placing them upon an alleged physiological foundation. In this attempt the writer has been rather more successful than authors of other similar books in that for his physiology he has turned mostly to capable physiologists. He has not, however, entirely escaped the pitfall into which authors of this sort of books are prone to fall, namely, to quote as authoritative the physiological conclusions reached by known bunglers or unheard of amateur investigators.

The book is out of date in the assumption made that the function of the adrenal glands is determined essentially by their output of adrenin. The author is distinctly more hospitable to alleged efficacy of various glandular products in everyday therapy than an unprejudiced study of the literature on organotherapy justifies. The book concludes with a brief bibliography, the citations of which include some of the best and some of the poorest literature which has been published in the field covered.

Anyone desiring that impossible entity, a brief and easy introduction to endocrinology, will find himself less likely to be misled by this than by most other books along this line.—R. G. H.

STUDIES IN DEFICIENCY DISEASES. Robert McCarrison. Oxford University Press, N. Y. & Lond., 1921. 270 p.

This book on a very timely subject is based upon the investigations of the author in addition to the correlation of already existing facts. The objects of the study were "to find out how the body goes sick in consequence of deficient and ill balanced food" and to deduce therefrom what forms of sickness in the human subject may reasonably be attributed to, or connected in their origin with, such foods. McCarrison feels that the health of the gastro-intestinal tract is dependent on the adequate provision of accessory food factors. A state of ill health of this

tract may be a prescorbutic manifestation of disease due to insufficient vitamin intake, especially when there is excess of fat or starch or both in the food.

He thinks that vitamines in their action resemble hormones whose function is to stimulate metabolism. Disturbances of metabolism are bound up and in considerable measure are dependent on the disturbance of endocrine function which results from the same cause. It seems that both the functional perfection and correlation of the endocrine organs are dependent upon a properly balanced and vitamine-containing food supply. Dietetic deficiency means endocrine insufficiency.

Effects of food deficiency on the organs of internal secretion are shown by atrophy of the thymus, spleen, testicles, ovary, thyroid and parathyroid and by hypertrophy of the adrenals and pituitary. This hypertrophy may perhaps be compensatory. An adequate supply of vitamins is essential to perfect nutrition of the heart and kidneys.

The book is a valuable addition to the literature on the vitamines and deficiency diseases, especially in relation to the endocrine system.—M. B. G.

DAS HYPOPHYSENGEWICHT BEIM MANNE UND SEINE BEZIENHUNGEN. Dr. Paul Petersilie, Langensalza, 1920. Verlag von Wendt & Klauwell, 26 p.

The author examined the hypophyses of 189 men who died during the war. The average weight was found to be 620 mg., the lowest 300 mg. and the highest 900 mg. There was found no relation between its weight and the locality in which the person lived. The data indicate that up to the 30th year the weight increases, then remains unaltered until the 40th year, when it gradually diminishes. Small persons generally have a small hypophysis and tall persons have a larger one. Usually the greater the weight of the gland, the greater the compactness of the bone structure. Thus there seems to exist a relation between the length of the body and the weight of the gland, but not between the weight of the body and the weight of the gland. When geographical influences are eliminated we may say that a heavy hypophysis is accompanied by a light *thyroid* and vice versa. When the hypophysis is heavy, the *testicles, pancreas* and kidneys are also heavy. No relation exists between the weight of the hypophysis and the *adrenals*.—J. K.

EIN FALL VON BEIDERSEITIGER HODENOERDOPPELUNG (A CASE OF FOUR TESTICLES). Dr. P. Kern, Langensalza, 1921. Verlag von Wendt & Klauwell, 19 p.

In this small brochure a good description has been given of a man with four testicles, hypospadia penis and spina bifida

occulta. The patient is still living. Sexual desires were normal, not exaggerated. The spermatozoa were larger than normal. This is the sixth case reported. (See Day, Endocrin., **3**, 95.)—J. K.

DIE ERFOLGE DER STEINACHBEHANDLUNG BEIM MENCHEN. Dr. L. Lenz and Dr. P. Schmidt, Berlin, 1921. Verlag von G. Tiemsen, 32 p.

A popular little book, written without critical acumen. The authors believe rejuvenation to be absolutely certain. Operation is also advised for fatigue, palpitations, giddiness and headache. The publication of this type of popular medical literature is deplorable.—J. K.

ENDOCRINOLOGIA. Livini, Rondoni, Peppere, Pende & Coronedi, Milano, Italy, 1922. Istituto Sieroterapico Milanese, 350 p.

The volume comprises a group of lectures on endocrinology given to newly graduated doctors. The anatomy and embryology, physiopathology, anatomo-pathology, the relations of the endocrine glands to nervous and mental pathology and the therapeutic applications are discussed in a clear and concise way and great care is taken by each of these professors not to overindulge in personal views. The object of this book and the steady warning given to young practitioners not to be misled by untimely enthusiasm are especially worthy of praise.

—G. V.

LES GLANDES SURRENALES ET L'HYPOPHYSE. Dr. R. Porak, Paris, 1922. Librairie Octave Doin, 103 p., 8°.

This work includes three distinct studies: the first, of Addison's disease; the second, of the therapeutic action of pituitary extracts; and the third, upon adrenal insufficiency, but a common purpose reigns throughout the study, that of physiological pathology. "Today," says the author, p. 67, "where clinicians abuse their diagnosis of adrenal insufficiency, it is well to recall experimental labors and through their light to criticize clinical observations." It is in this critical spirit that the author examines the question studied. And this criticism, both wise and prudent, is due to the fact that he always refers to the teachings of physiological pathology, hence his description of the data bearing upon acute adrenal insufficiency, slow insufficiency, and the bearing of these upon adrenal insufficiency in the clinic of human diseases, its rapid and subacute forms. In all cases the gravity of the disease does not appear at all connected with the diminution of adrenalin in the pathological adrenals. Adrenal insufficiency, in fact, appears as such only in the clinic, and the

treatment by means of adrenalin has never in reality ameliorated these morbid conditions any more than it has ameliorated Addison's disease. Thus, in the same spirit, Porak discusses pituitary opotherapy, showing that no absolute conclusion may be drawn from the numerous cases in which it has been used, and showing particularly that even if we are familiar with the pharmacologic effects of these extracts, their biological meaning has entirely escaped us.—E. G.

GHIANDOLE A SECREZIONE INTERNA. A. Peppere. Vol. 8 in Trattato di Anatomia Patologica, Pio Foà. Torino, 1922. Unione Tipografica Editrice Torinese. 300 p., 8°.

The subject is exhaustively treated with objective views inspired by thoroughly scientific criticism. The vast bibliography shows that none of the foreign publications has been overlooked and may prove of some interest by bringing the rich scientific contribution on the part of the Italian scientists to the notice of the readers. The widely known name of Prof. P. Foà is in itself a guarantee of the exceptional value of this work. The first volume, on Blood and Hematopoietic Organs, by Prof. Foà, has, in less than six months, reached its second edition.

—G. V.

THE FOLIA ANATOMICA JAPONICA. Vol. 1, No. 1, March, 1922.

A new journal devoted to the publication of original material of anatomical research, macroscopic and microscopic anatomy, embryology, experimental morphology, physical anthropology, macroscopic and microscopic methods of investigation, etc. Under the management of K. Okajima, Keio Universität, Tokyo.—R. G. H.

ARCHIVES OF OCCUPATIONAL THERAPY. The official organ of the American Occupational Therapy Association. Vol. 1, No. 1. Feb., 1922.

A new journal devoted to the publication of the fundamental data which are now scattered in many periodicals or which now lack the proper means of dissemination. It will be of interest to not only the medical and surgical world, but also to those interested in social service, to the psychologist, to business organizations interested in the educational recreational value of occupational therapy, etc. Edited by Wm. R. Dunton, Jr., M. D. Published bimonthly by Williams & Wilkins Company, Baltimore, Md.—R. G. H.

Abstract Department

(ADRENIN: THYROID) The physiological action of the proteinogenous amines. V. Vegetative nervous system and metabolism (Beiträge zur Kenntniss der physiologischen Wirkung der proteinogenen Amine. V. Vegetatives Nervensystem und Stoffwechsel). Abelin (J.), Biochem. Ztschr. (Berl.), 1922, **129**, 1-49.

A study of the action of adrenalin, thyramine, phenyl-ethylamine, tyramine thyroid substance, cholin, acetylcholin, histamine, pilocarpin and atropin on the gas exchange of the white rat, and the effect of tyramine and phenylethylamine on the gas exchange of a thyroidectomized dog. All the compounds with the exception of histamine and acetylcholine increased the gas metabolism and frequently produced diuresis. Glycogen mobilization, **hyperglycemia** and **glucosuria** occurred. Tyramine and phenylethylamine are additive in their action on metabolism, for when sub-effective doses of either are administered together with sub-effective doses of thyroid substance there is produced a marked increase in gas exchange. These observations make it appear probable that the action of the thyroid on metabolism is only an expression of a generalized influence on the vegetative nervous system and that this is of great significance in the regulation of the kind and degree of total metabolism. The dose and the method of administration are important factors, for smaller doses are effective when the compounds are given per oram. Histamine has no effect on the gas exchange, while acetylcholin produced a significant reduction.—F. S. H.

(ADRENIN) Treatment of sciatica (Behandeling van ischias). Adels (M. H. J.), Vox med. (Utrecht), 1922, **22**, 82-83.

In very rebellious cases of sciatica the author recommends the injection of 20 mg. of novocain and 1 mg. of adrenalin into the nerve.
—J. K.

Very severe paroxysmal adynamia with ADRENAL insufficiency (Paroxysmale schwerste Adynamie bei Insuffizienz der Nebennieren). Bauer, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

Adynamia may be the only symptom of insufficiency of the adrenals. The author observed, for example, a patient who had attacks of weakness, lasting for ± 2 hours, during which he was not able to stand. In one case an amyloid degeneration of the cortex was found, but no important changes in the medulla.—J. K.

(ADRENIN: PITUITRIN) Studies on the visceral sensory nervous system. XII. The response of the isolated oesophagus of the frog and the turtle to certain drugs. Bercovitz (E.), Am. J. Physiol. (Balt.), 1922, **60**, 219-233.

Carlson and Luckhardt have reported that stimulation of the peripheral vagus in the turtle causes inhibition of the circular neuromuscular mechanism of the oesophagus in its upper two-thirds, and contraction of the longitudinal system in the region of the cardia. The present paper reports the results of an attempt to throw further light on this subject by the use of a number of so-called neurotropic and myotropic drugs. Among these were adrenalin and pituitrin. In the frog's oesophagus adrenalin caused a uniform inhibition of the longitudinal system. In 66% the circular system was stimulated; in 33% it was inhibited. Armour's pituitary liquid caused uniform inhibition of the circular and longitudinal systems. In the turtle adrenalin caused a profound and lasting stimulation preceded by temporary inhibition.—T. C. B.

(ADRENIN) How the blood calcium is changed by drugs (Der Calcium spiegel im Blute und seine Beeinflussung durch verschiedene Gifte). Billigheimer (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 256-258.

In 15 patients adrenalin 13 times caused a temporary decrease of the amount of calcium in the blood. The decrease was most marked in patients in whom the change in pulse, **blood sugar** and **blood pressure** was most marked also.—J. K.

The effect of ADRENALIN on healthy persons. Bjure (A.) & Svensson (Y.), Upsala Läkaref. Förh., 1921, **26**, 1-23; J. Aug. Hammar, Festskrift. Each article is paged separately.

The authors, at intervals of a month, injected epinephrin into five healthy medical students, once in a dose of 0.5 mg. and twice of 1 mg. A great many clinical examinations were made with the following results. The effects of epinephrin injections vary considerably in different healthy persons and in the same person at different times. There was always found a rise of the content of blood sugar with a maximum in about three-quarters hour and a lymphocytosis with the maximum of about one-half hour after the injection. Frequently a rise of the blood pressure and the pulse rate with the maximum one-half hour after the injection was observed. The red blood corpuscles showed in one experiment an evident rise persisting at least 3 hours. The quantity of urine and the absolute quantity of NaCl in the urine were often increased. Sometimes, however, the urine and the NaCl were decreased. No definite changes were noted in the respiration rate, the percentage of NaCl in the blood or the haemoglobin.—H. B.

Intracardial injection of ADRENIN in an infant (Intrakardiale Adrenalinjektion bei einem vier Monate altem Säugling). Bliedung, Klin. Wchnschr. (Berl.), 1922, **1**, 196; München. med. Wchnschr., **69**, 309-310.

In a child of 4 months 0.2 cc. of a 1% solution of adrenin was injected into the heart, which had discontinued beating during narcosis. There was complete recovery.—J. K.

Developmental disturbances and arrests of the ADRENAL in Addison's disease (Entwicklungsstörung und Entwicklungshemmung der Nebennieren bei Addison'scher Erkrankung). Bloch (R.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67**, 71-113.

Processes resembling disturbed or arrested development of the adrenal are to be observed in certain cases of Addison's disease. The author finds the medulla enlarged and the cortex lacking or degenerated.—W. J. A.

The analgesic action of ADRENIN in certain forms of ophthalmic neuralgia (L'action analgésique de l'adrénaline dans certaines formes de névralgie ophthalmique). Bonnefou, Compt. rend. Soc. de biol. (Paris), 1922, **86**, 374-376.

In cases of neuralgia of the ophthalmic connected with an infectious condition in which the painful crisis is preceded by a vasomotor aura, the instillation into the conjunctival sac of a few drops of adrenalin, 1:1000, may avert the crisis. If the instillation is too tardy, after lachrymation, photophobia and periocular injection has set in, the adrenalin does not avert the crisis, but notably shortens its duration. If given during a neuralgic attack its effect is nearly null. A case is cited.—T. C. B.

Acetonuria and glycemia after injection of ADRENIN in dysentery (Azetonurie und experimentelle Adrenalinglykämie bei Ruhr). Buttenweiser, München. med. Wchnschr., 1922, **69**, 83.

In 2 patients with acetonuria in whom adrenalin was injected there was no hyperglycemia and in 5 others it was seen in a very light degree. When 100 gms. of glycose was given before the injection of adrenalin, hyperglycemia became much more marked.—J. K.

(ADRENIN) On the automatic movements of the isolated iris. Cate (J. T.), Versl. d. k. Akad. v. Wetensch. Wis-en natuurk. Afd. (Amst.), 1921, **30**, 143-144.

By employing a method for magnifying contractions of iris muscle 16 times, the author found that a supply of oxygen causes a lasting contraction of the muscle, but a diminution in rhythmic movements. Pilocarpine hastens the movements, adrenaline slows them. Pilocarpine and choline both increase the strength of the contractions, while adrenaline weakens and atropine stops them.

—Physiol. Abst., **7**, 17.

Rôle of the vegetative system in the production of hypertonia of voluntary muscles. I. Action of ADRENIN and of calcium chloride. II. Action of eserin and of atropin. III. Action of ADRENIN, eserin and atropin in successive injections. IV. Rôle of the sympathetic and parasympathetic respectively. Idea of amphotonia (Rôle du systéme végétatif dans le production de l'hypertonie des muscles volontaires. I. Action de l'adrénaline et du chlorure de calcium. II. Action de l'ésérine et de l'atropine. III. Action de l'adrénaline, de l'ésérine et de l'atropine, employées en injections successives. IV. Rôle respectif du sympathique et du parasympathique. Notion de l'amphotonie). Daniélopolu (D.), Radovici (A.) & Carniol (A.), Compt. rend. Soc. de biol. (Paris), 1922, **86**, 625-634.

A series of four papers dealing with tonus of striped muscle. Of endocrine interest in that adrenalin was one of the substances used to show the innervation of voluntary muscle by the autonomic system.—T. C. B.

(ADRENAL) The influence of x-rays on the endocrine glands (Beeinflussung endokriner Drüsen durch Röntgenstrahlen). David, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

Animal adrenals were directly exposed to x-rays (the organs were exposed by an operation). Sometimes the adrenalin content was increased, sometimes lowered. This problem should be studied by application of known quantities of x-rays to the naked organs of internal secretion.—J. K.

(ADRENAL) Addison's disease with pluriglandular insufficiency (Addisonsche Krankheit mit pluriglandulärer Insuffizienz). Deusche, München. med. Wchnschr., 1922, **69**, 373.

A man of 43 with Addison's disease showed the following symptoms: very low blood pressure; pigmentation; asthenia; cachexia; thin hair and beard; dry atrophic skin; no sexual desires; small thyroid; normal testicles and hypophysis (as far as may be judged by clinical examination); and pernicious anemia.—J. K.

(ADRENAL) Morbus Addison. Fahr, Klin. Wchnschr. (Berl.), 1922, **1**, 501; München. med. Wchnschr., 1922, **69**, 227; Deutsche med. Wchnschr. (Berl.), 1922, **48**, 613.

A woman of 53 had bronzed skin, normal blood pressure and cachexia. At autopsy it was found that the adrenals weighed 1 and 0.5 gm.; the medulla was normal; the cortex, atrophic.—J. K.

Is extirpation of an ADRENAL in epilepsy justified (Kritisches zum Artikel Specht's: Is die Nebennierenexstirpation bei Epilepsie berechtigt)? Fischer (H.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 113-115.

Fischer found that after removing an adrenal it was not possible to produce spasms in an animal by amyl nitrite, but Specht could not confirm this. Specht made the mistake of administering pure amyl nitrite without air, causing the animal to suffocate and get spasms with or without adrenals.—J. K.

(ADRENALS) Experimental studies on spasms (Tierexperimentelle Krampfstudien). Fischer (J.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 591-595.

H. Fischer has reported experiments showing that ablation of one adrenal is followed by a lowered sensibility for spasmodic poisons and toxins. His work has not been confirmed by Specht, whose experiments have been abstracted in Endocrinology. J. Fischer now states that Specht has never properly read the publications of H. Fischer. Specht seems to believe that all spasms are identical—that there is no difference between epilepsy and other spasms. Ablation of an adrenal is an operation without risk and as cases have been described in which this operation has been performed with some success and as there is no other treatment, it should be tried in epilepsy. Specht's experiments with amyl nitrite have been carried out with poor technique. In many experiments the animals did not inhale amyl nitrite, but nearly suffocated because the mask was too small. The use of fresh amyl nitrite is of great importance. To test the sensibility of an animal after ablation of an adrenal, it is necessary to wait until the animal is quite recovered from the shock of operation and narcosis. When all these precautions are taken the animals show a lowered sensibility after ablation of an adrenal. Before the ablation the animals often lose consciousness; when amyl nitrite is administered after the ablation this is rare. When 0.2 mg. of adrenalin per kg. body weight or 0.2 mg. of **hypophysis** per kg. body weight was injected into a normal rabbit 10 minutes before the inhalation of amyl nitrite, spasms were much more intense, causing many of the animals to die.—J. K.

The function of the ADRENALS. IV. The rôle of the ADRENALS in the vasomotor phenomena of asphyxia. Purely nervous mechanism of these phenomena (La fonction des surrénales. IV. Du rôle des surrénales dans les phénomènes vaso-moteurs de l'asphyxie. Mécanisme purement nerveux de ces phénomènes). Gley (E.) & Quinquaud (A.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 22-34; abst., Physiol. Abst., **7**, 51.

In dogs whose bulbo-medullary axis has been completely destroyed there is no indication of the well known cardiovascular reaction of asphyxia and no modification of arterial pressure. However, the vessels in this condition remain sensible to the excitant which acts directly on their musculature to the direct excitation of the different nerves as to different poisons—to **adrenalin** in particu-

lar. After division of the two large splanchnics, an operation which renders all secretion of adrenalin impossible, the vasomotor reaction of asphyxia is not modified. After double adrenal ablation the same is true. Vasomotor reactions are not, then, event partially of humoral origin (under the influence of adrenal secretion); they are of central nervous origin.—R. G. H.

Relation between the changes in the H-ion concentration in the vena porta and the hyperglycemia after ADRENIN administration (Ueber den Zusammenhang zwischen H-ionkonzentrationsverschiebung im Pfortaderblute und der Hyperglykämie nach Adrenalininjektion). Gottschalk (A.), München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

When the vena porta is ligated hyperglycemia occurs. The author was able to prove that this was not due to a changed circulation in the liver (no details are given). When alkali is given the effect of adrenalin on the **blood sugar** is much less marked. The respiration of the liver tissue is markedly diminished by injection of adrenalin. Adrenalin thus acts directly upon the liver cells. —J. K.

The relation of the ADRENALS to fatigue. Hartman (F. A.), Waite (R. H.) & Powell (E. F.), Am. J. Physiol. (Balt.), 1922, **60**, 255-269.

See Endocrin., **6**, 511-518.—T. C. B.

Perfusion of the medulla of the terrapin (Pseudomys troosti) with ADRENALIN. Heinekamp (W. J. R.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 131-134.

These experiments were carried out as a reply to Bush (see Endocrin., **5**, 481). The author found that adrenalin, perfused through the medulla of Pseudomys troosti, causes partial or complete inhibition of the heart.—F. A. H.

ADRENAL extirpation and epilepsy (Nebennierenexstirpation und Epilepsie). Heymann (E.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 255-257.

Treats only the technique of the operation.—J. K.

Tumor of the right ADRENAL (Tumor der rechten Nebenniere). Horner, Klin. Wchnschr. (Berl.), 1922, **1**, 707.

A short note. Hematuria was the only symptom manifested. Death resulted from metastases in the lungs.—J. K.

Energometric studies on the influence of ADRENIN on the circulation (Energometrische Untersuchungen über die Wirkung des Adrenalins auf den Kreislauf). Hotz (A.), Deutsches Arch. f. klin. Med. (Leipz.), 1922, **138**, 257-269.

In very detailed and exact experiments on healthy children the author studied the influence of adrenalin on the blood vessels. It has been proved in animals that injection of adrenalin is followed by a rise of the pulse volume of the peripheral arteries. The same was proved in case of the arteria brachialis of children, showing that the blood vessel becomes larger under the influence of adrenalin. The systolic blood presure rises, the pressure of the wall of the vessel ("Wanddruck") rises also, but the diastolic pressure often sinks. This last fact is probably due to an increased flow of blood to the right heart. Cloetta and Anderes were able to prove in animals that when adrenalin is injected the size of the lungs is increased by this increased flow of blood to the right heart. Therefore, Hotz supposes that the same occurs in man and that this explains the diastolic blood pressure after the injection of adrenalin.—J. K.

A criticism on Specht's article: "Is ADRENAL ablation in epilepsy justified?" (Kritischez zu dem Artikel "Ist die Nebennieren-exstirpation bei Epilepsie berechtigt?"). Kersten (H.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 482-485.

The author criticises Specht's article (Endocrinol., 1922, **6**, 130). Both the form of the mask with which the amyl nitrite is given and the number of drops administered are highly important. It is necessary also that it be fresh, for old solution contain HNO_2 and ethyl valerinate and are inactive. Normal rabbits, after ablation of an adrenal, have much less severe spasms when they inhale amyl nitrite than before this ablation. During pregnancy the adrenal system becomes hypertrophic and Kersten observed that his pregnant animals showed spasms sooner when this substance had been administered than did the normal controls. Hypertrophy of the adrenals is also seen after **castration** and in these cases, too, spasms after inhalation of amyl nitrite occur earlier than in normal animals. Kersten states that ablation of an adrenal causes a diminished sensitiveness to spasmodic substances and that hypertrophy of the adrenals is followed by an increased sensitiveness for such substances.—J. K.

The influence of ADRENIN on the excretion of uric acid (Die Ausscheidung der Harnsäure unter Einflusz von subkutanen Adrenalingaben). Krauss (E.), München. med. Wchnschr., 1922, **69**, 761.

Though the blood contains much uric acid in primary hypertonia, the urine contains but little. When adrenalin is injected in healthy persons the excretion of nitrogen, urea, creatinin and NaCl is augmented; the excretion of uric acid is diminished as soon as the blood pressure rises. The excretion of water may be increased or diminished. When the blood pressure is high after the injection of adrenalin the serum contains large amounts of uric acid. The excretion of the uric acid seem to depend upon the blood pressure.—J. K

The influence of veratrin and EPINEPHRIN on skeletal muscle. Kruse (T. K.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 266.

Epinephrin did not produce veratrin-like effects on frog's skeletal muscle. Solutions up to 0.01 per cent were employed.—F. A. H.

(PITUITRIN, EPINEPHRIN) Certain aspects of the part played by the liver in the regulation of the blood volume. Lamson (P. D.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 267-268.

If hemoglobin can be used as an index of the fluid content of the blood, epinephrin would increase the rate of fluid loss, largely due to its action in the liver. Pituitrin would decrease the rate of fluid concentration from the circulation very greatly, holding fluid injected into the circulation for over three hours. It also overcomes the action of epinephrin. The increased rate of fluid loss after epinephrin has been accounted for by constriction of the hepatic veins and an increased filtration pressure in the liver.—F. A. H.

The influence of ADRENIN on the permeability of the sarcolemma (Über die Einwirkung des Adrenalins auf die Permeabilität von Muskelfasergrenzschichten). Lange (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 70.

A short note. Adrenalin diminishes the permeability of the tissues between the muscles fibres.—J. K.

The action of ADRENIN on muscular excitability and fatigue (Action de l'adrénaline sur l'excitabilité musculaire et sur la fatigue). Lapicque (M.) & Nattan-Larrier (M.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 474-476.

Experiments were made on the muscle and nerve of frogs, toads, crawfish, snails, frog's heart, etc. The conclusion is that adrenalin diminishes the "chronaxie" of all the tissues considered, as well as the fatigue following repeated excitation.—T. C. B.

A hemorrhagic cyst of the ADRENAL cortex (Beitrag zur Kenntnis der Struma suprarenalis cystica haemorrhagica). Laxh (C. H.), Beitr. z. klin. Chir. (Tübing.), 1922, **125**, 467-475.

A cystic tumor was removed from a woman of 31. It contained cholesterol and erythrocytes. Cortex tissue of the adrenal was found in the wall. Only 10 similar cases have been published. —J. K.

(ADRENIN) The action of some drugs on the vessels, studied with the capillary miscroscope (Mikrocapillarbeobachtungen über die Wirkung eingiger Gefäszmittel). Moog (O.) & Ambrosius (W.), Klin. Wchnschr. (Berl.), 1922, **1**, 944-947

Adrenalin causes a narrowing of the arteriolae and the capillaries. Only the arterial part of the capillaries shows a contraction. The blood stream becomes slower and the tissues get less blood. When the capillaries are studied with the skin microscope after the injection of adrenalin they have a granular aspect. Contraction of the capillaries occurs only when there is a blood stream in these capillaries. When, for example, the blood stream is temporarily arrested by tying a cord around a limb, adrenalin does not produce contraction. When the vessels are damaged by a want of oxygen or by a large quantity of carbonic acid the influence of adrenalin is much less intense. Adrenalin is not decomposed by the tissues as is proved by the fact that when injected into a limb tied by a cord, which, a few minutes later is taken away, the action of adrenalin is quite normal. In the same way, when adrenalin is injected and another limb is tied, it does not act on the vessels of that limb. If 10 to 20 minutes later the cord is taken away the action of the adrenalin on the arterioles may be seen by the skin microscope.—J. K.

Disturbed formation of adrenin in the ADRENALS due to external causes, and its biological significance (Störungen der Adrenalinbildung in den Nebennieren unter äusseren Einflüszen und ihre biologische Bedeutung). Peiser (B.), Klin. Wchnschr. (Berl.), 1922, **1**, 628-629.

The author found the adrenaline content of 150 adrenals to be about 30% less than before the war. By experiments on guinea pigs he was able to prove that this was due to underfeeding.—J. K.

The vasoconstrictor action of ADRENIN and strychnine. Plumier (L. L.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 434-445.

The author studied the action of these compounds by measuring simultaneously the pressure from the central end of a carotid artery and the peripheral end of the two crural arteries, after having sectioned the nerves of one of the paws. This method devised by Nolf (Bull. Acad. roy. de méd. de Belg., 1902, p. 895) does not determine whether the vasoconstrictor substance acts on the neural centers or on the vessel walls. It was shown that strychnine apparently acts on the former and adrenalin on the latter, as was to be expected.

—Chem Abst.

Changes in the H-ion concentration after injection of ADRENIN (Aenderungen in der Wasserstoffionenkonzentration nach Adrenalininjektion). Pohle, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

In both the vena porta and the vena hepatica the H-ion concentration was largely increased after injection of adrenalin. This increase was preceded by the rise of the blood sugar.—J. K.

The cardio-vascular action of ADRENIN in man. Difference of physiological effect in the healthy and pathological states (L'action cardio-vasculaire de l'adrénaline chez l'homme. Différence de l'effet physiologique a l'état sain et à l'état pathologique). Porak (R.), J. de physiol. et de path. gén. (Par.), 1920, **18,** 1194-1202.

In the normal subject the rise of blood pressure for a given dose varies according to the individual. This fact must be taken into account in testing the reaction to adrenalin in disease. Thus the indications of disorders of internal secretion may be modified by those due to infections of the vascular or nervous system.

—Physiol. Abst., **6,** 72.

On the mechanism of the ADRENAL function (Sur le méchanisme de la fonction surrénale). Rebello (S.) & Pereira (M. de M.), Compt. rend. Soc. de biol. (Par.), 1922, **86,** 325-327.

It has been shown that adrenalin when injected into the lower extremity of a frog, attached to the body only by the sciatic nerve, exerts its effect at a distance. The following hypothesis is given. Histologically and embryologically the suprarenal medulla must be considered an annex to the sympathetic, or as a part of that system differentiated for certain functions. Adrenalin is easily oxydized. Its existence in the blood beyond the vena cava inferior is uncertain. It is difficult to admit a sympathicotonic effect by way of the arteries of a substance so sensitive to oxygen, and it seems simpler to admit that adrenalin, produced by the chromaphil cells, exercises an exciting action on the nerve terminations, which is continuous, and is transported to a distance by maintaining the sympathetic tonus.—T. C. B.

Test for ADRENIN (Über Adrenalin). Russmann, Klin. Wchnschr. (Berl.), 1922, **1,** 654.

A 4 cc. slightly acid solution of adrenalin, 1 drop of saturated $HgCl_2$ solution, 3 drops of saturated sulfanilic acid and 1 cc. of a solution of KIO_3 boiled together for 1 minute produces a brown color. The reaction is positive with a solution of adrenalin of 1:50 million. (The concentration of the KIO_3 is not given.)—J. K.

Reply to Fischer's criticism on my article, "Is ADRENAL ablation justified in Epilepsy?" (Erwiderung auf die Kritik Fischer's zu meinem Artikel "Ist die Nebennieren exstirpation bei Epilepsie berechtigt?"). Specht (O.), Zentralbl. f. Chir. (Leipz.), 1922, **49,** 402-403; Beitr. z. klin. Chir. (Tübing.), 1922, **125,** 347-367.

Specht's original article has been abstracted in this Journal, 1922, **6,** 130. Fischer has criticised Specht for giving amyl nitrite to his animals in such a way as nearly to suffocate them. Later on, however, Specht used exactly Fischer's technique. The results were the same in both cases. Specht therefore persists in his previous conclusions.—J. K.

On the relationship between the ADRENAL gland and the THYROID. Scrimger (F. A. C.), Canad. M. Ass. J. (Montreal), 1922, **12**, 316-317.

The two recognized groups of goitre are cited, exophthalmic and the toxic adenoma. A third group is set up, similar to the exophthalmic in some respects but lacking the exophthalmos. Microscopically, areas are "indistinguishable from the generalized hyperplasia associated with true Graves' disease." It is suggested that, in this third group the thyroid and the adrenal or other ductless glands are diseased, while in the other groups the thyroid alone is diseased. Evidence is gleaned from the literature to prove the point.—J. H.

Complete ADRENAL insufficiency. Soler (F. L.), Rev. méd. de Hamburgo, 1921, **2**, 107-109.

The conclusions are: (1) Complete removal of the adrenals in dogs does not lead to a functional cessation of motility nor to an auto-curarisation. (2) The toxic results affect chiefly the brain cortex, giving rise to symptoms similar to those which can be induced hypnotically.—Ber. ü. d. ges. Physiol., **10**, 97.

The function of the ADRENAL cortex (Ueber die Funktion der Nebennierenrinde). Stephan (R.), München. med. Wchnschr., 1922, **69**, 339-342.

Stephan examined a large number of women during, or a short time before, the onset of the **menopause** and nearly always found a marked hypertension and a slight polycythemia (5.8-7 millions of erythrocytes). The blood pressure and the number of erythrocytes do not run parallel. When the left adrenal in such women was exposed to intense x-rays, no influence was seen on the blood pressure, but the number of erythrocytes always decreased and stayed normal for about a week. The same was seen in hypertension with sclerosis of the kidneys. In a woman suffering from a cancer of the stomach the author exposed the left adrenal to the same amount of x-rays. Necropsy showed a necrosis of the cortex with a normal chromaffin tissue. The cortex seems to be radiosensitive, while the medulla does not. Therefore, it is probable that the number of erythrocytes has some relation to the cortex, as this number is diminished by the action of x-rays. It is an important question whether the polycythemia of the menopause is due to an increased formation or a diminished destruction of red blood cells. Stephan has been able to prove in other experiments that the amount of proteolytic enzymes in the blood runs parallel with the destruction of red cells. In the menopause these enzymes are diminished and, therefore, it is stated that the polycythemia is due to a diminished hemolysis. After x-ray treatment the proteolytic enzymes in the blood rose, hemolysis increased, and the number of red blood cells

decreased. As this hemolysis is a function of the spleen it is stated that it is under the control of the adrenal cortex.—J. K.

The action of drugs on the output of EPINEPHRIN from the ADRENALS. VIII. Morphine. Stewart (G. N.) & Rogoff (J. M.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 59-85.

Morphine, administered subcutaneously or intravenously caused in cats an increase in the rate of output of epinephrin, sometimes as much as ten times the initial rate. These results were obtained in animals under the influence of ether or urethane. The symptoms produced by morphine in non-anesthetised cats seem to be independent of the adrenals, for removal of one adrenal and part of the other and denervation of the remainder, does not appear to modify them. Morphine caused little or no increase in the epinephrine output in dogs.—F. A. H.

The influence of muscular exercise on normal cats compared with cats deprived of the greater part of the ADRENALS, with special reference to body temperature, pulse and respiratory frequency. Stewart (G. N.) & Rogoff (J. M.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 87-95.

No difference in rectual temperature, pulse rate, respiratory rate, resistance to fatigue or recovery from fatigue, was observed in cats with one adrenal and a large part of the other removed or the second one denervated, as compared with normal cats, when subjected to prolonged muscular exercise. After severe muscular exertion there is a definite although not great depletion of the epinephrin store in an adrenal with intact nerve supply, using a denervated adrenal as a control. Considerable exertion, falling short of great fatigue may not cause depletion.—F. A. H.

The influence of morphine on normal cats and on cats deprived of the greater part of the ADRENALS, with special reference to body temperature, pulse and respiration frequency and blood sugar content. Stewart (G. N.) & Rogoff (J. M.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 97-130.

The marked hyperthermia caused by morphine in cats has been studied in connection with the development of the general symptoms, the changes in the pulse and respiratory frequency and the sugar content of the blood. It has been observed that there is no close association between the hyperthermia and the hyperglycemia, or even the degree of muscular activity. The hyperthermia and the general symptoms develop in the same way, and reach the same intensity in cats from which the greater portion of the adrenal tissue has been removed and the remaining fragment denervated, as in normal cats. An increase in blood sugar was observed after asphyxia, provided there was a storage of glycogen. Morphine did

not cause an increase in blood sugar in these animals with deficient adrenals. The authors did not find that adrenalectomized rats succumbed to a very much smaller dose of morphine than normal rats.
—F. A. H.

Über ADRENALIN. Stuber, Russmann & Proebsting, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

The authors have invented a new chemical method for the estimation of extremely small quantities of adrenalin. No details are given.—J. K.

ADRENAL incretory and direct nervous secretory mechanism of hyperglycemia by splanchnic excitation. Experimental dissociation (Double méchanisme, glyco et adrénalino—secrétoire de l'hyperglycémie par excitation splanchnique. Dissociation expérimentale). Tournade (A.) & Chabrol (M.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 315-316.

By means of an anastomosis between the right suprarenal vein of one dog (B) with the jugular of another (A) (see Endocrinol., **6**, 285), it is possible to divert the blood of B into the circulation of A. There is then an increase in glycemia in both dogs. This is interpreted as demonstrating that hyperglycemia is due to the secretion of adrenalin in the case of A, and an effect on the liver in the case of B.—T. C. B.

A note on ADRENALIN hyperglycemia in man. Ulrich (H. L.) & Rypins (H.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 215-220.

The authors were not able to produce polycythemia by adrenalin through loss of fluid into the liver as observed in dogs. However, on account of the severe systemic reaction, they were not able to use more than 0.33 cc. of a 1:1000 solution intravenously in a 70 kilo man. This is about 1/180 of the dose which has been used in dogs. Adrenalin hyperglycemia in man is not explained on the basis of a change in blood concentration, because it is independent of such change.—F. A. H.

Influence of ADRENIN in DIABETES (Über die probatorische Adrenalinwirkung beim Diabetiker). Veil (W. H.) & Reisert (A.), Deutsches Arch. f. klin. Med. (Leipz.), 1922, **139**, 235-244.

When adrenalin is injected subcutaneously in normal persons, four blood sugar curves may be constructed, as follows: (1) a flat line, gradually rising to ± 160 mg. in 1 hour; (2) a line with a sharp angle, reaching 160 mg. in ± 30 minutes, 180-230 mg. in ± 1 hour and then falling rapidly; (3) a high, long plateau; (4) a high line, rapidly rising, and after 10 minutes a rapid fall. The first two are normal lines; 3 and 4 are seen in increased irritability of the

nervous system ("Reizkurven"). The authors then constructed curves in 12 cases of diabetes. In one very light case, curve 1 was seen. In 5 very nervous cases, types 3 or 4 were seen. All the patients died. In 6 cases a different curve was found. First there was a very slight decrease, then a retarded rise, the maximum blood sugar being reached in 4 hours in one case: These 6 cases with nervous manifestations were found to have secondary diabetes. One patient had an encephalomalacia of the medulla oblongata, one a tumor of the base of the brain, one probably had a pineal disease, one an encephalomalacia from arteriosclerosis, a fifth developed diabetes after apoplexy and the last had syphilis. The authors further studied the vasomotor reaction in diabetes after ingestion of adrenalin. The reaction was normal in cases with normal blood sugar curves. In serious cases (with "Reizkurven") the intensity was much diminished—as was seen in the cases of secondary diabetes. Glycosuria occurred in slight degree or not at all in cases showing normal blood sugar tracings; in cases with "Reizkurven" there was a parallelism between the amount of blood sugar and glucosuria. In cases of secondary diabetes with retarded glycemia reaction there was no relation between blood sugar and glucosuria. The glucosuria was sometimes very marked when the glycemia was low; and high glycemia was not always accompanied by glycosuria. Further injection of adrenalin increased the acidity of the urine; acidosis occurred or was increased and the CO_2 tension in the alveolar air was diminished.—J. K.

The action of ADRENAL on the skin glands of the toad. Wastl (H.), Ztschr. f. Biol. (München. u. Leipz.), 1922, **74**, 77-80.

The subcutaneous injection of 1 cc. of a 1:10,000 or 1:20,000 solution of adrenaline induces secretion of the skin glands of the toad.—Chem. Abst., **16**, 1623.

The pathology of DIABETES. 1. Hydropic degeneration of the islets of Langerhans after partial pancreatectomy. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 5-41.

This is the first of a series of papers by the author on the pathology of experimental diabetes. In it are reported the histological changes in the cells of the islets after partial removal of the pancreas. Hydropic degeneration is proved to be a specific diabetic condition produced by overstrain of the cell function. The first positive vacuolation appears in from four days to one week and this is maximal at the end of one month. After six or eight weeks the beta cells may disappear entirely as the animal becomes completely diabetic, whereas the alpha cells show no changes. The difference in the behavior of the partially and totally depancreatized animals taken together with this difference in appearance of the two types of cells indicates that the beta cells furnish the internal

secretion lacking in diabetes, while the alpha and other cells of the pancreas furnish material essential for other life processes. This is the first anatomical evidence of injury to cells due to overstrain of their incretory function and is offered as a means of diagnosing active diabetes histologically.—I. M.

The pathology of DIABETES. 3. Nervous influence in the etiology of experimental diabetes. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 53-73.

The object of this investigation was to study the effect of nervous influences in diabetes by various procedures. Normal and diabetic animals exposed to various forms of shock failed to show any changes attributable to this factor. The Bernard puncture in a partially depancreatized animal caused fatal glycosuria. Enervation and grafting studies showed the sugar tolerance to be undisturbed by the procedure, and grafted pancreas showed the specific vacuolation of the islands under the same conditions as in the pancreas with nerves and other connections intact.—I. M.

The pathology of DIABETES. 4. The rôle of hyperglycemia in the production of hydropic degeneration of islands of Langerhans. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 75-88.

The purpose of this series of experiments was to determine the effects of different blood sugar levels upon the cells of the islands. In a portion of the experiments the effects of intense hyperglycemia, produced by intravenous or oral administration, was studied on normal and experimentally diabetic dogs with negative results. Although glycosuria was produced, no hydropic changes or vacuolation occurred in the cells. Hypoglycemia, produced by phlorizin administration, had no effect in producing or repairing changes in the cells. The author concludes that there is some other factor than hyperglycemia that is responsible for the hydropic changes in the diabetic islets.—I. M.

The pathology of DIABETES. The influence of circulatory alterations upon experimental diabetes. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 89-95.

This group of experiments was intended to show any possible relation of circulatory or vasomotor disturbances to the pathology of diabetes. By operative methods the blood supply to and from the pancreas remnant in experimental animals was regulated and varied. No changes in the appearance of the cells or in the functional activity of the islands could be observed following such procedures.—I. M.

Experiments on carbohydrate metabolism and DIABETES. 4. Dextrose-nitrogen ratios in partially DEPANCREATIZED dogs. Allen (F. M.) & Wishart (Mary B.), J. Metabolic Research (Morristown), 1922, **1**, 97-107.

This paper deals with the D:N ratio, especially in depancreatized animals. Not all animals with the pancreas completely removed show a permanent 2.8:1 ratio, but the authors believe that those not showing the total ratio are as completely diabetic as those with this ratio. Some only partially depancreatized animals show the total ratio. The D:N ratio cannot, therefore, be an infallible test as to whether the pancreas has been completely removed. A total D:N ratio even for a short time in the partially depancreatized dogs indicates a fatal outcome. In human cases of diabetes this is not so, perhaps because a part of the disturbance is functional and capable of correction, whereas it is all organic in case of the experimental diabetes. Partially depancreatized animals can be distinguished from those totally depancreatized by a smaller loss in total sugar and nitrogen, by a lower total basal metabolism, by better nutrition and by much longer lives.—I. M.

The pathology of DIABETES. 6. PANCREATITIS in the etiology of experimental diabetes. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 165-192.

The experiments reported in this paper were undertaken to reproduce more nearly the clinical pathology of diabetes in the presence of large masses of apparently healthy pancreatic tissue. It has previously been observed by the author that spontaneous diabetes occasionally occurs in old and obese dogs and exceptionally in experimental animals in which atrophy and fibrosis have occurred in large pancreatic remnants. In the present experiments a successful attempt was made to reproduce these conditions by causing an acute pancreatitis by mechanical trauma or occlusion of the pancreatic circulation for a time. Marked power of tissue regeneration was observed in most cases, but in a few fibrosis and atrophy occurred with clinical diabetes as an end result. The conclusion is drawn that fibrosis may occur in the pancreas as evidence of past injury, but does not indicate a progressive inflammatory condition. The fate of the islands depends upon the occurrence of hydropic degeneration or its not occurring—hence the value of prolonged dietary control.—I. M.

The pathology of DIABETES. 7. Microscopic studies of the PANCREAS in clinical diabetes. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 193-219.

This paper considers in some detail the microscopic findings in the pancreas in human diabetes and compares them with the picture in experimental diabetes in animals. While most frequently the

human diabetic pancreas at autopsy does not show the typical hydropic degeneration of the islet cells seen in experimental diabetes, hydropic changes probably have occurred at an early stage with subsequent repair or regeneration. Acute infections or toxic processes or functional strains must increase the intensity of the hydropic degeneration and so increase the severity of the diabetes progressively. Identical degrees of hyperglycemia and glycosuria cause more rapid downward progress in diabetic children than in diabetic adults, perhaps because of the greater susceptibility of the child's pancreas to functional strain. With hyperglycemia but a glycosuria the diabetes of childhood becomes worse, but in adults the condition tends to remain stationary or to improve. All pancreas sections examined showed some signs of abnormality in the islands, as fibrosis, hydropic or hyaline degeneration, or quantitative reduction in the islet tissue. Severe cases with marked diabetic symptoms at time of death showed hydropic changes, whereas old, severe cases without diabetic symptoms, in which the patient died of starvation from lack of food tolerance, showed a scarcity of islands and fibrosis. Functional deficiency apparently does not cause death, and further organ changes can be halted or delayed by dietary control.—I. M.

The pathology of DIABETES. 8. The microscopic pathology of the PANCREAS in 570 unselected hospital cases. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 221-250.

This paper deals with the pathology of the pancreas in 21 diabetic and 549 clinically nondiabetic cases. All of the diabetic and 48 per cent of the nondiabetic cases showed some kind of lesion of the pancreas. Many of the latter group had associated cirrhosis of the liver, gall stones and syphilis. Focal necroses, acute pancreatitis, hemorrhages, fatty infiltration and fibrosis constitute the chief lesions in the nondiabetic cases. Diminution in the number of islets and hydropic or hyaline degeneration of the remaining islets with or without diffuse fibrosis is the specific condition of diabetes, although a large functional element is also recognized.—I. M.

The pathology of DIABETES. 9. Literature and discussion. Allen (F. M.), J. Metabolic Research (Morristown), 1922, **1**, 251-279.

This paper summarizes the author's observations on the pathology of diabetes. It is pointed out that the pancreas is one of the most commonly diseased organs in the body from infections local and generalized, intoxications of various kinds by way of the ducts, the blood or the lymphatics, from neoplasms, etc. There is said to be no uniform pathological change pathognomonic of diabetes. A uniform functional alteration of the islands is probable. Hydropic changes in the islet cells indicate active diabetes and occur especially in severe youthful cases. The author holds that the majority of diabetic cases are not inherently progressive and can be controlled indefinitely by proper treatment. The chief causes

of a forward course in any case are intercurrent infections and hydropic changes from over-taxed function. The author denies a selective preservation of the islands of Langerhans after pancreatic duct ligation.—I. M.

Alcohol in the DIABETIC diet. Allen (F. M.) & Wishart (Mary B.), J. Metabolic Research (Morristown), 1922, **1**, 281-306.

This investigation, in which ethyl alcohol was employed to increase the total caloric value of the diabetic diet, was undertaken to further test Allen's original contention that the diabetic subject is limited in his "power to metabolize calories as such" as well as to metabolize carbohydrates. It is held that the assimilative power is injured or diminished when the total caloric tolerance is exceeded by any food, even fat and alcohol. It was found that increases above the caloric tolerance in the total caloric intake due to fat or alcohol increase alone (the total available glucose remaining the same), caused hyperglycemia, glycosuria and acetonuria. Ethyl alcohol is not converted within the body into glucose or acetone. The increased caloric intake in these fairly severe diabetic patients failed to cause gain in weight or nutrition, but, on the other hand, lowered the assimilation power still further.—I. M.

(DIABETES) Treatment of diseases of metabolism with mineral waters (Behandlung von Stoffwechselkrankheiten mittels Thermalwasser). von Benczur, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 543.

Health resorts may have effective results only in fat patients with diabetes, and this is usually slight. Drinking water with laxative properties may also be useful.—J. K.

(DIABETES) The distribution of blood sugar in the circulating blood (Ueber die Verteilung des Blutzuckers im strömenden Blute). Csáki (L.), Wien. Arch. f. inn. Med., 1922, **3**, 459-468.

The author estimated the blood sugar with Bang's micromethod. To obtain blood plasma, 5 cc. of fresh blood were centrifugated for 5 minutes and the plasma was immediately used to estimate the sugar. In this way the blood sugar and plasma sugar could be compared, while defibrination and the adding of anti-coagulation substances was avoided. Csáki proved that the corpuscles contain little or no sugar. In diabetes, however, the corpuscles may contain even large quantities of sugar. When in normal persons the blood sugar is increased, the corpuscles remain sugar free. In diabetes the corpuscles have a marked permeability for sugar. This difference between normal and diabetic blood is not changed by the absence or presence of acetone or diacetic acid.—J. K.

DIABETIC edema and acidosis (Diabetisches Oedem und Acidose). Földes (E.), Wien. Arch. f. inn. Med., 1922, **3**, 469-498.

Many patients with diabetes show fluctuations in their weight, due to varying degrees of edema. Every day the author gave to 9 patients ±50 gm. of sodium bicarbonate. Six of these patients had diabetes with or without mild acidosis; one had **Graves' disease**; the two others suffered from combined sclerosis (sclerose enplaques). None developed edema and none showed spontaneous variation of weight. In cases with marked acidosis the ingestion of comparatively small doses of sodium bicarbonate was often followed by an increase in weight and edema. There are, however, cases with severe acidosis in which no edema is seen after ingestion of $NaHCO_3$. Many of these cases showed very severe polyuria. When the acidosis disappears, the possibility of edema from ingestion of $NaHCO_3$ disappears also. The author formulates the following as a law: "Without acidosis, no diabetic edema." When a patient with acidosis has no edema, edema may develop from three causes: (1) sudden increase of the acidosis; (2) diminishing of diuresis (as is seen on fasting days or when a strict diet is given); (3) when much salt ($NaHCO_3$) is given. The refractive index of the blood serum sinks when edema develops, and rises when edema disappears. This proves that the protein concentration of the serum changes when edema occurs. The author was able to prove that this was not caused by changed quantity of protein but only by variations of the quantity of water. In cases of diabetic edema, hydremia always exists. It is probable that acidosis also has an influence on the kidneys and facilitates the development of edema. In diabetes without acidosis the size of the red corpuscles is the same as in normal persons. In severe acidosis they are generally larger than in health. When such patients ingest $NaHCO_3$ until the urine becomes alkaline or until its acidity is largely diminished, the size of the corpuscles diminishes also. The average size of the corpuscles is thus a method for measuring acidosis. The author has proved that the corpuscles show an increased size in diabetics in whom edema easily develops. Földes has found, too, that when so much $NaHCO_3$ is given that the urine becomes alkaline, no edema is seen; edema may develop when less $NaHCO_3$ is given, so that acidosis does not disappear.—J. K.

The use of oats in DIABETES (Het gebruik van haver bij suikerziekte). Foyer (A.), Nederl. Tijdschr. v. Geneesk. (Amst.), 1922, **66**, (I) 1420-1423.

A short general review. Nothing new.—J. K.

The presence of pyrocatechinic acid in normal and DIABETIC urine (Eine Untersuchung über das Vorkommen von Brenztraubensäure in normalen und Diabetekerharn). Fricke (R.), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1922, **119**, 39-45.

Negative results.—F. S. H.

(DIABETES) Glycemia and glycosuria. Graham (G.), Lancet (Lond.), 1921, **i**, 951-955.

This is the first of a series of three lectures delivered before the Royal College of Physicians on the subject of diabetes. This paper deals almost entirely with a review of the physiological aspects of carbohydrate metabolism. In discussing the fate of the sugar present in the blood, the author describes experiments made upon himself in which he showed fairly marked variations in individual response to a given dose of sugar at different times, for example, before and after a holiday. The difference in tolerance for different sugars is pointed out also. Regarding the mechanism regulating the amount of sugar in the blood, he discusses the glucose mobilizing activity of the **adrenals**, the **thyroid** and the **hypophysis** and the antagonistic activity of the **pancreas**. Of particular interest is the review of Cohnheim's work on the substance in muscle tissue found necessary for sugar storage, of the work of Dakin and Dudley on a substance necessary to prevent conversion of muscle sugar into lactic acid (anti-glyoxose) and of Clark's observations on the substance in muscle which enables them to oxidize sugar.—I. M.

Treatment of DIABETES with diet and mineral waters (Diabetes therapie durch Diät und Mineralwässerkur). Graul, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 543; Klin. Wchnschr. (Berl.), 1922, **1**, 917.

A vegetarian diet is the best for diabetes. The water of Neuenahr brings about effective results in diabetes, not only while the patient is in Neuenahr, but also later.—J. K.

Modern views on DIABETES (Diabetes in moderner Beleuchtung). Heiberg (K. A.), München. med. Wchnschr., 1922 **69**, 731-733.

In children with diabetes, harmless infections (bronchitis, a simple cold) may markedly diminish carbohydrate tolerance. When a diet rich in calories is given, much more food passes through the body without being properly digested than when a diet poor in calories is given. Therefore, the best diet would be one as poor as possible in calories. Treatment with alimentary rest, as taught by the American investigators, shows enormous progress in the treatment of diabetes.—J. K.

Simplification of the Woodyatt method for calculating the optimal DIABETIC diet. Holmes (W. H.), J. Am. M. Ass. (Chicago), 1922, **78**, 22-23.

Four tables are presented to simplify the calculation of the optimal diabetic diet, as recently recommended by Woodyatt.

—W. M. A.

Methods of precision in DIABETES: A new instrument. John (H. J.), J. Am. M. Ass. (Chicago), 1922, **78**, 103-105.

The use of a vacuum bleeding tube containing picric acid solution for blood sugar determination is described. It is claimed that it is useful and reliable even when a delay of two or three days intervenes between the collection of the specimen and its analysis; thus making available distant laboratory facilities.—W. M. A.

Vitamines and DIABETES (Vitamine und Diabetes). Klotz & Höpfner, München. med. Wchnschr., 1922, **69**, 465-466.

Vitamines influence metabolism. The calcium metabolism in rickets is improved when fresh extracts from sweet potatoes, turnips or carrots are given. In an experiment upon one patient, a girl of 12, the authors found that extracts from sweet potatoes in not too large quantities diminished the sugar in the blood and urine, but that yeast had no influence. However, Borutteau (Biochem. Ztschr. (Berl.), 1918, **88**, 420) proved by much more extensive experimentation the existence of antidiabetic substance in these vegetables and in yeast also.—J. K.

Polyuria and DIABETES (De polyurie bij suikerziekte). Koopman (J.), Nederl. Tijdschr. v. Geneesk. (Amst.), 1922, **66**, (I) 1338.

A short note. Data reported in Endocrinol., 1922, **6**, 48.

The dietetic treatment of DIABETES (Einige Bemerkungen über die diätische Behandlung des Diabetes). Krehl (L.), Fortschr. d. Med. (Berl.), 1922, **40**, 309-310.

In diabetes, restriction of food is necessary; not only fat, carbohydrates and proteins but also vegetables (salad) must be limited. It is very important that the patients be weighed regularly. Not only should a diet be selected that keeps the urine sugar free, but it is highly important to study the blood sugar and to give a diet in which, if possible, blood sugar is normal.—J. K.

High blood pressure and DIABETES (Hypertoni och sockersjukdom). Kylin (E.), Hygiea (Stockholm), 1922, **84**, 49.

Kylin determined the blood pressure in 71 cases of diabetes mellitus. Some of his readings were obtained while the patients were still in the hospital, others, when the patients returned to have their pressure taken. Most observations were made in the afternoons. In the diabetics under 40 years of age, the blood pressure was normal, while after 40 hyperpiesis was the rule. Thus 75% had a systolic pressure of over 160 mm. of Hg., and 50% had 180 and over. Kylin suggests that high blood pressure and reduced carbohydrate tolerance go hand in hand, and since some cases of hypertension also have lymphocytosis he is inclined to believe that

high blood pressure is due to an endocrine deficiency, possibly a hypofunction of the sex glands.—D. J. G.

Fasting treatment of DIABETES (Les cures de jeune chez les diabètiques). Labbé (M.), Bull. et. mém. Soc. med. d. hop. de Par., 1921, **45**, 689-699.

In diabetes where denutrition has not occurred the fasting method of treatment leads to good results. The glucosuria disappears, no acidosis appears if it has not already been present, although some slight acetone and diacetic acid excretion may take place. There is some loss of nitrogen and body weight. The arterial pressure is but little less during the treatment. In cases where emaciation is present the fasting treatment affords only a passing relief.—F. S. H.

Overnutrition with fat and alcohol in severe DIABETES. Leclercq (F. S.), J. Metabolic Research (Morristown), 1922, **1**, 307-317.

The authors attempted to determine the effect of increasing the total caloric intake by administration of alcohol and fat in two fairly severe cases of diabetes. The intake of protein and carbohydrate was kept at a constant level, representing the tolerance of the patients for these foods. In no instance was the weight or strength increased and no beneficial clinical change was found to take place. After a few days of improvement, the patients began to feel weak and uncomfortable. Hyperglycemia followed both fat and alcohol ingestion, and so did not help for long. A further impairment of assimilation resulted, due to excess of calories.—I. M.

(DIABETES) The inhibiting influence of lumbar puncture on glycosuria (L'influence frénatrice de la ponction lombaire sur la glycosurie). Lhermitte (J.) & Fumet (C.), Compt. rend. Soc. de biol. (Paris), 1922, **86**, 479-480.

The subtraction of a small amount of spinal fluid by lumbar puncture in diabetics determines a notable diminution in the excretion of glucose completely independent of all modifications of regime. This action is temporary, but may last several days.—T. C. B.

Xanthoma DIABETICORUM: report of case. Lyon (D. M.), Edinb. M. J., 1922, **28**, 168.

Apart from the skin lesion Lyon's case presents several points of unusual interest. All the symptoms and the examinations of the blood and urine suggested a serious type of diabetes mellitus. The patient had polyuria reaching 7,000 cc., glycosuria of 5 per cent, and daily waste of about 300 gm. carbohydrate, high fasting level of the blood sugar, 0.388 per cent, and very low carbohydrate tolerance as shown by the greatly exaggerated postprandial rise in the blood sugar. There was obvious difficulty in dealing with the fats

ingested. Such a serious state of affairs in a man, aged 25, would suggest a very bad prognosis, and yet he returned to almost perfect health. From this it would seem that in making a prognosis less weight should be given to the evidence of the severity of the disease and more to the amount of improvement that the patient is capable of under treatment. This improvement has been maintained for at least nine months.—J. Am. M. Ass., **78**, 1761.

Hypertonia and DIABETES (Über Hypertonie und Zuckerkrankheit. Marañón (G.), Zentralbl. f. innere Med. (Leipz.), 1922, **43**, 169-176.

As both diabetes and hypertonia are mostly seen in patients over 40, one might believe that age was the cause of the coincidence. It is remarkable that in many patients there is marked hypertonia some time before glucosuria is found. Marañón states that in these cases hypertonia often gradually diminishes when the diabetes develops. When a patient of about 40 begins to show an increased blood pressure and blood sugar, a decreased **carbohydrate tolerance,** and a changed reaction after injection of **adrenalin,** it is probable that diabetes will set in. Fourteen out of 22 cases of hypertonia without glucosuria showed hyperglycemia. There are cases of hypertension in which this symptom is only temporary and disappears with treatment or even without treatment. Patients with hypertonia and **adiposity** often become diabetic; it is the same with those with hypertonia who complain of severe itching. Some of these patients have hyperglycemia. It may be the same in case of furunculosis or neuralgia. The author concludes that in a certain number of cases of diabetes there exists a "preglycosuric stage" of hypertension with other symptoms, such as itching, neuralgia, furunculosis, etc.—J. K.

The pathology of DIABETES. 2. Granule stains of the islands of Langerhans of the diabetic and non-diabetic pancreas. Martin (W. B.), J. Metabolic Research (Morristown), 1922, **1**, 43-52.

In this paper the author describes the alpha and beta cells making up the islets and the special staining technique by which the two types are distinguished. The eccentrically placed alpha cells with their oval vesicular nuclei and basophilic granules are greatly in the minority, while the centrally placed beta cells with rounded nuclei and acidophilic granules surround the blood capillaries and make up the greater part of the islets. Four stages of alteration in the cells are described as taking place in diabetic animals with final disappearance of the beta cells. Corresponding stages are not found in all cases of human diabetes, the beta cells appearing normal in some, which indicates that some functional alteration must be assumed as the basis of diabetes in man.—I. M.

(DIABETES) Sugar metabolism (Beitrag zum Zuckerstoffwechsel). Meier, München. med. Wchnschr., 1922, **69**, 138-139.

The author gave his patients, on an empty stomach, 20 gms. of glucose and one hour afterwards, 100 gms. more. In normal persons after the dose of 100 gms. no further increase in blood sugar is seen; but a second increase was observed in patients with icterus, nitrobenzol poisoning, obesity due to **endocrine insufficiency**, and serious neurosis. In diabetes, even a second dose of 10 gms. caused a marked rise.—J. K.

DIABETES und Balneologie. Minkowski (O.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 475-477; Klin. Wchnschr. (Berl)., 1922, **1**, 917.

A stay in a health resort may have a good effect in diabetes. To explain this, Minkowski suggests the following: The general condition of the patient is improved by favorable hygienic, climatic, psychical influences, etc., which have an influence on the diseased organs. Mineral water increases the production of certain enzymes or hormones, influences the velocity of reactions ("Reaktionsgeschwindigkeit") and contains substances, which can, at least partly, take the place of substances, the want of which causes diabetes. Since, however, these things are purely theoretical, it is advisable to send patients only to those health resorts in which a good diabetic treatment is prescribed.—J. K.

DIABETES mellitus en DIABETES INSIPIDUS. Munk (J.), Nederl. Maandschr. v. Geneesk. (Leiden), 1921, **2**, 253-268.

A description of 4 cases. The first was a girl of 4 with extremely malignant diabetes mellitus. The second was a girl of 5½ with diabetes insipidus cured by the oral administration of hypophysis tablets. The third and fourth were girls of 5½ and 9 with diabetes mellitus. The last two had "diathèse neuro-arthritique" in the family.—J. K.

The importance of the alimentary experiment, especially the reaction of glycemia, for the functional study of SUGAR METABOLISM (Ueber die Bedeutung des Alimentärversuches, speziell der "glykamischen Reaktion" für die funktionelle Prüfung des Zuckerstoffwechsels). Offenbacher (R.) & Hahn (R.), Arch. f. Verdauungskr. (Berl.), 1922, **29**, 193-219.

The authors estimated the amount of blood sugar with the stomach empty; then 50 gm. of glucose in 300 gm. of tea was given and every hour the sugar in the blood and urine was determined. In some cases, no changes in the blood sugar were seen after one hour, but in other healthy persons a moderate increase was still seen. These were usually nervous persons. In neurasthenia a rise

during the first hour of ± 100% or more was seen and in the second hour this rapidly fell to, or even under, the normal blood sugar content. In 3 cases of **Graves' disease** glucosuria was seen. All of the 7 cases of this disease examined had low blood sugar content on an empty stomach; 6 showed a very marked rise (much more than 100%) of blood sugar the first hour after the ingestion of the glucose. In all cases the hyperglycemia disappeared after two hours. In only one case was the blood sugar high on an empty stomach, and in this case the blood sugar remained unaltered by ingestion of 50 gm. of carbohydrate.—J. K.

A chart for the rapid estimation of Woodyatt's optimal DIABETIC diet. O'Hara (D.), J. Am. M. Ass. (Chicago), 1922, **78**, 1124.

With the body weight and glucose tolerance known, the chart permits a rapid calculation of the optimal arrangement of the protein, fat and carbohydrate in the diet.—W. M. A.

Factors in development of DIABETIC acidosis (Ueber die Faktoren die für die Entwicklung der Azidose bei Diabetes von Bedeutung sind). Petrén, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

In health as well as in diabetes, acidosis is caused by a lack of carbohydrate in the diet. In diabetes, however, acidosis occurs also when the patient takes more than a certain amount of nitrogen in the form of proteins. Proteins raise the **blood sugar**; fats have no influence.—J. K.

Syphilitic DIABETES. Rathery (F.) & Fernet (P.), Bull. et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 661-667.

A report of a case of diabetes cured by antisyphilitic treatment.—F. S. H.

Treatment of DIABETES (Behandlung des Diabetes). Richter (P. F.), Ztschr. f. ärztl. Fortbild. (Jena), 1922, **19**, 33-41.

A general good review, without new data.—J. K.

Pathogenesis and treatment of DIABETES (Wesen und Behandlunge des Diabetes). Schreiber, München. med. Wchnschr., 1922, **69**, 139.

No new data are given.—J. K.

Experiments on carbohydrate metabolism and DIABETES. The influence of glucose ingestion on diuresis and blood composition in non-diabetic and diabetic persons. Sherrill (J. W.) & John (H. J.), J. Metabolic Research (Morristown), 1922, **1**, 109-129.

The authors studied the effect of glucose ingestion on urinary output, blood volume, hematocrit readings, hemoglobin and blood

sugar in 19 persons, a part of whom were diabetic and the remainder normal. They found that in the majority of cases oliguria and a decrease in hematocrit reading accompanied the hyperglycemia, whereas diuresis followed upon the appearance of a hydremic plethora as the blood sugar returned to the normal level. Hemoglobin values decreased with the hyperglycemia, as did the hematocrit, but both returned to normal following the diuresis. In one control case 10 gm. of sodium chloride was ingested with similar results.

—I. M.

Dietetic treatment of DIABETES (Die Aufgaben der Diätbehandlung in der Diabetestherapie). Strausz (H.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 546-549.

A general review.—J. K.

A peculiar disturbance of carbohydrate metabolism and its relation to DIABETES (Über eine eigenartige Störung des Kohlenhydratstoffwechsels and ihre Beziehungen zum Diabetes mellitus. Eine klinisch-experimentelle Studie). Wagner (R.) & Parnas (J. K.), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **25**, 361.

The authors have investigated a case of glycosuria in a girl of 8½ years who had been under observation since the age of 4. The principal physical sign was a greatly enlarged liver. It was that the morning urine gave an intense reaction for acetone compounds. With the administration of both starch and sugar there was glycosuria. The remarkable feature of the case was that, on examination of the blood, it was found that during fasting the fluid was entirely free from sugar. After food, an extreme hyperglycemia took place. In the fasting stage injections of adrenalin did not produce the hyperglycemia which occurs in normal subjects under similar conditions. Hence the disturbance is not due to a mobilization of glycogen, but is due to a lack of mobilizable carbohydrate. In this case the administration of protein, lactates, glycerine, and amino-acids after fasting raised the content of sugar in the blood. Thyroid in fairly large doses was without effect: with larger doses lipemia, lipuria, and staetorrhoea occurred. During one day the normal quota of sugar appeared in the blood. The authors look upon the case as one of azooamylia, i. e., a lack of function on the part of the liver to store up sugar in the form of glycogen. On the other hand, the regulating mechanism is absent which in the normal fasting subject catabolizes protein in order to keep the sugar content of the blood at its normal level, and in cases of diabetes leads, in spite of the absence of carbohydrates in the food, to a hyperglycemia. This process, however, can be replaced by the administration of **thyroid**, and thus shows the importance of this gland for sugar metabolism in that the thyroid regulates the endogenous protein metabolism and prepares this protein for the formation of sugar. In the relation of **pancreas** and thyroid, the latter acts as a

brake to excessive pancreatic activity. It is difficult in the present case to make out clearly the relations of pancreas, liver and thyroid. It is possible that with the dysfunction of the liver there is an independent disturbance of the thyroid which leads to an inhibition of endogenous protein breakdown; or the lack of liver function and activity of the thyroid are determined by a disturbance of the pancreas.—Med. Sc., **6**, 161.

DIABETES INSIPIDUS of infundibular origin. Anatomo-clinical study (Le diabète insipide d'origine infundibulaire. Etude anatomo-clinique). Lhermette (J.), Compt. rend. Soc. de biol. (Paris), 1922, **86**, 579-581.

Whether diabetes insipidus is of hypophyseal or nervous origin is still under discussion. Hitherto we have possessed no facts absolutely demonstrating the origin of polyuria in man, because the majority of observations are either incomplete, or too complex to be utilized. The present paper describes a case of polyuria in a man of 65, under observation for 17 months. He had chronic aortitis and incipient tabes. The daily quantity of urine was 4 to 4.5 liters. There was a positive Wassermann in the blood and cerebro-spinal fluid. Specific treatment was of no avail. The autopsy showed a **syphilitic** basilar meningitis involving the tuber cinereum and the infundibulum. The **hypophysis** was intact. There was granular degeneration of the cells of the nuclei of the tuber, chromotolysis of the paraventricular nuclei and the supra-chiasmatic nuclei were vacuolated. The hypophysis, **thyroid** and **suprarenals** were unaltered. These facts justify the conclusion that polyuria in man, as in experimental animals, may be due to lesions in the vegetative center of the base of the brain and not to lesions of the hypophysis. There is a short discussion by G. Roussy.—T. C. B.

DIABETES INSIPIDUS. Lorant, München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

When purin free food was administered to patients with diabetes insipidus, thus causing nitrogen equilibrium, their **uric acid metabolism** became abnormally high. A short note.—J. K.

The INCRETION of the tonsils (Zur Frage der inneren Sekretion der Tonsillen). Amersbach & Königsfeld, Klin. Wchnschr. (Berl.), 1922, **1**, 501; Deutsche med. Wchnschr. (Berl.), 1922, **48**, 542-543.

Fleischmann has stated that the tonsils have an endocrine function because it is possible to extract from them a substance which reduces $AuCl_3$. The authors consider this observation as of no significance because nearly all tissues contain such substances.—J. K.

Principal questions in ENDOCRINOLOGY (Prinzipielle Fragen zur Lehre von der inneren Sekretion). Asher (L.), Klin. Wchnschr. (Berl.), 1922, **1**, 105-108.

A general review without new facts.—J. K.

(ENDOCRINE GLANDS) Pathology of the sympathetic (Pathologia do sympathico). Barros (F.), Arch. Rio Grandenses de Med. (Porto Alegre, Brazil), 1922, **3**, 51-56.

A general review of the interrelations of the endocrine glands, the sympathetic nervous system and various pathological manifestations.—F. S. H.

ENDOCRINE factor in dental caries. Broderick (F. W.), Proc. Roy. Soc. Med. (Lond.), 1922, **15**, 22-40.

Hypotheses not supported by experimental evidence.
—Physiol Abst., **7**, 49.

The action of thallium on the ENDOCRINE organs (Die Wirkung des Thallium auf den endokrine System). Buschke (A.) & Peiser (B.), Klin. Wchnschr. (Berl.), 1922, **1**, 995.

More than 20 years ago Buschke demonstrated that animals lost their fur when thallium was given. Since there were no changes in the skin the author believed that thallium had a central action. These studies have been repeated and it has been proved that when thallium is given to young animals growth is retarded or ceases completely. In adult animals sexual desires disappear and there exists a complete atrophy of the **testicle.** In the **adrenals** no adrenalin, or only traces of it are found. Sometimes cataracts were seen, perhaps due to an abnormal function of the **parathyroids.** It is not yet certain whether changes occur in the **thyroid.**—J. K.

(ETIOLOGY) Myasthenia gravis: A therapeutic and clinical study. Dana (C. L.), J. Am. M. Ass. (Chicago), 1922, **78**, 261-263.

Fourteen personal cases are reported with a general discussion of the disease. The clinical and pathological grounds for belief in an endocrinal etiology are briefly referred to, without experimental evidence.—W. M. A.

The influence of x-rays on the ENDOCRINE glands (Der Einflusz der Röntgenstrahlen auf inkretorische Drüsen). David, Klin. Wchnschr. (Berl.), 1922, **1**, 1025.

No specific data are given.—J. K.

Influence of x-rays on the ENDOCRINE ORGANS (Ueber die Beeinflüssung endocriner Drüsen durch Röntgenstrahlen). David, München. med. Wchnschr., 1922, **69**, 526.

No details are given. The necessity of exact dosage of x-rays is stated.—J. K.

(ENDOCRINE ORGANS) Glioma and status hypoplasticus. Diamantopoulos (H. S.), Klin. Wchnschr. (Berl.), 1922, **1**, 708.

In a boy of 13 with hypoplastic **gonads** and polyuria, postmortem examination showed glioma which had destroyed the corpora mammillaria and tuber cinereum, hypoplasia of the lymph tissue, and atrophy of the **thyroid** and **testicles.** No particular changes in the **hypophysis** were found.—J. K.

Functional diagnosis of diseases of the ENDOCRINE organs (Funktionelle Diagnostik der Erkrankungen der Blutdrüsen). Falta, Klin. Wchnschr. (Berl.), 1922, **1**, 1028.

Some general remarks without new data.—J. K.

ENDOCRINE ORGANS in woman (Innersekretonische Vorgänge bei der Frau). Franz, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 544; Klin. Wchnschr. (Berl.), 1922, **1**, 970.

Menstruation and **ovulation** are quite different things. Menstruation is caused by the endocrine function of the **ovary.** X-radiation of the ovary before menstruation has no influence on menstruation; when the ovaries are exposed to x-rays after menstruation the next menstrual period is missed. In pregnancy the size of the **thyroid** and the pars anterior of the **hypophysis** may increase enormously. Hypertrophy of the **mammae** and lactation do not depend upon the ovary. The only ovary preparation of therapeutic value is ovoglandol, and this only because of its large calcium content. —J. K.

(ENDOCRINE) Intoxication in adults, arteriosclerosis and organotherapy with "animasa" (Nährschäden Erwachsener, Arteriosklerose und deren organo-Therapeutische Beeinflüssung durch "Animasa"). Funck (C.), Arch. f. Verdauungskr. (Berl.), 1922, **29**, 167-170.

The author believes that a pathological **protein metabolism** may be responsible for many cases of **diabetes, hypertonia, glycosuria** and beginning **arteriosclerosis.** Extract of the intima and meadia of blood vessels is combined with a substance procured by destruction of the protein of blood and is called "animasa." When given by mouth it brought very good results in many cases of arteriosclerosis. One case is quoted in which the blood pressure sank from 205 mm. to 160 mm. No convincing data are adduced.—J. K.

The influence of CO_2 baths on the INTERNAL SECRETION of the skin (Die Wirkung der Kohlensauren Bäder die innersekretorische Funktion der Haut). Groedel, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 544; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

CO_2 baths have good effect in endocrine disturbances **(diabetes, Graves' disease)**. A relation between the endocrine glands and the skin is highly probable as many endocrine disturbances produce cutaneous symptoms. When extracts of skin are injected they produce the same symptoms as extracts of **adrenals.** Therefore, the author concludes that the endocrine function of the skin is proved, that probably the CO_2 baths primarily act on the internal secretion of the skin and that this produces a change in the other endocrine glands.—J. K.

(ENDOCRINE ORGANS) Experimental studies on the pathogenesis of gout (Experimentelle Beiträge zur Pathogenese der Gicht). Gudzent & Keeser, Ztschr. f. klin. Med. (Berl.), 1922, **94**, 1-11.

During their studies on gout the authors estimated the quantity of uric acid in different organs. They found that the fatty tissue did not contain uric acid; very small quantities were found in the **thyroid,** muscle and lung; there was more in the **testicle,** bile, kidney and brain; large quantities were found in the liver, spleen and **pancreas.**—J. K.

Glimpses into ENDOCRINOLOGY. Hamilton (W. F.), Canad. M. Ass. J., 1922, **12**, 209-214.

A case is cited of a male, aged 25, 4 feet 7 inches in height, and weighing 76 pounds. Development was normal until he was ten years old. For fifteen years he had headache and development was slow, especially of the genitalia. Autopsy showed a tumor of the **pituitary,** choriod plexus, atrophy of the **thyroid** and **testes, adiposity** and effeminate characteristics. A second case, a male, at 5 years of age showed characteristics of a young adult in voice, teeth and genitalia. Operation revealed a tumor of the **adrenal** cortex. The patient again became practically a normal child. A third case, that of a girl 8 years old, is cited. For two years she had typical symptoms and laboratory findings of **diabetes insipidus.** Two years later, symptoms of a brain tumor developed. Four years after onset a postmortem showed a tumor occupying the space of all the structures in the circle of Willis. The author says the case is not at all in favor of the view that diabetes insipidus is a hypophyseal syndrome.

—J. H.

Histological studies on the ENDOCRINE ORGANS in psychical disturbances (Histologische Untersuchungen der innersekretorischen Drüsen bei psychischen Erkrankungen). Fauser (A.) & Heddacus (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 374.

Will be published in detail in the Ztschr. f. d. ges. Neurol. u. Psychiat.—J. K.

Amphibian metamorphosis and INTERNAL SECRETIONS. Huxley (J. S.) & Hogben (L. T.), Proc. Roy. Soc. (Lond.), 1922, **93 B**, 36-53.

Metamorphosis takes place in Salamandra and Triton larvae in dilute iodine. In Axolotl, **thyroid** feeding causes more rapid metamorphosis (with exophthalmos), especially in young larvae, than does enforced air breathing; this is accelerated by rise of temperature. Free iodine or feeding on **prostate** or anterior **pituitary**, has no effect. In Necturns, thyroid diet for 7 months did not lead to somatic change. Pituitary diet (posterior lobe or whole gland) causes temporary dilatation, then contraction, of dermal melanophores in Axolotl; **adrenal** medulla produces temporary complete contraction. Administration of mammalian **pineal** causes transient contraction of these cells in frog tadpole, but not in Axolotl. The authors think probably the pineal ought to be admitted as a part of the endocrine system.—Physiol. Abst.

Influence of the ENDOCRINE organs on cell oxidations and heat regulation of the body (Wirkung von Inkreten auf die Zelloxydationen und den Wärmehaushalt des Organismus). Lipschütz, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1282.

Cell respiration was exactly measured. Extract of **pancreas** from an animal during hibernation diminished the respiration; extract of pancreas of a dog has no influence. **Thyroid** and **pineal** extracts increase respiration, **thymus** and cortex of **adrenal** decrease it. These last preparations diminish the temperature, while thyroid and pineal increase it.—J. K.

The influence of the ENDOCRINE ORGANS on the calcium content of human serum (Ueber den Kalziumgehalt des menschlichen Blutserums und seine Beeinflussung durch Störungen der inneren Sekretion). Leicher, München. med. Wchnschr., 1922, **69**, 331 and 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1282.

In **Graves' disease** and after ingestion of **thyroidin** the calcium content of the serum sinks; in **myxedema** it is high; after ingestion of **hypophysis** it sinks; in a case of tumor of the hypophysis it is high; ingestion of **ovary** causes decrease; castration causes increase; injection of **adrenin** causes a decrease and ingestion of **parathyroid**, an increase.—J. K.

(ENDOCRINE GLANDS) Treatment of epilepsy. Lopes (R. de S.), Brazil-med. (Rio de Jan.), 1922, **1**, 141.

Souza Lopes here discusses the accessory factors responsible for the epilepsy, the irritable motor and sympathetic systems, the toxemia, and the abnormal functioning of the endocrine glands. He describes the different signs of abnormal conditions in these various fields as the main problem in treatment of epilepsy.—J. Am. M. Ass., 1922, **78**, 1853.

(ENDOCRINE GLANDS) The next great advance in medicine. Macallum (A. B.), Canad. M. Ass. J., 1922, **12**, 202-208.

The opinion is given that the next great advance will be made by biochemists. The endocrine interest in this article is found in the discussion on constipation in which it is said that bacteria enter the blood stream and there ensues a hypertrophy of the **pituitary** and the **adrenals** with more or less atrophy of the other endocrinous glands.—J. H.

(ENDOCRINOLOGY) Animal experimentation and dental research. Mellanby (May), Dental Rec. (Lond.), 1922, **42**, 1-12.

A lecture dealing with previous work by the authoress and others on dogs, etc. Endocrine hypotheses still lack experimental evidence.—Physiol. Abst., **7**, 49.

(ENDOCRINE GLANDS) Glandular syndromes (Syndromas glandulares. Nonohay (U. de), Arch. Rio-Grandenses de Med. (Porto-Alegre, Brazil), 1922, **3**, 56-57.

A brief description of forms that are not new.—F. S. H.

Some aspects of ENDOCRINE therapy. Patton (A. B.), J. Med. Ass. Georgia (Augusta), 1922, **11**, 23.

A brief general discussion of the present status of organotherapy. The author concludes: "We know enough of the endocrines to have great faith in their ultimate effectiveness when we shall have learned to use them safely, and to realize that we really know little about them at present, that they are potent and dangerous, and that our information about them should come from the laboratory and clinic and operating room, and not from the manufacturer's advertising department."—R. G. H.

(ENDOCRINE GLANDS) Organ extract glycosurias (Ueber das Vorkommen von Organextraktglykosurien). Schenk (P.), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **24**, 208-213.

A report of the effect of the intramuscular injection into dogs of extracts of the **thyroid, testis, thymus, ovary, corpus luteum, placenta** and the various parts of the **pituitary.** In no case was glycosuria produced. The pituitary preparations and the extracts of the thyroid and thymus caused slight hyperglycemia.

—F. S. H.

Possible hormonic action of the CILIARY BODY (Su d'una possible azione ormonica dell'epitelio ciliare). Scalingi (N.), Riforma med. (Napoli), 1922, **38**, 345-346.

The author advances his hypothesis on the following premises: (a) the well known secretory activity of the ciliary epithelium, histologically and biologically demonstrated; (b) the non-existence of

a steady production of endocular fluid (function previously attributed to the ciliary process); (c) the hormonic functional connection between sympathetic and hormonic products, and, on the other hand, the arrested development of the eye following a spontaneous as well as an experimental lesion of the cervical sympathetic; (d) the deficient developments of the eye, or, at least, of its anterior segment, following certain inflammatory processes of early youth; (e) the bulbar atrophy and the sympathetic ophthalmia following "only" severe lesions of the ciliary processes.—G. V.

INNERE SEKRETION und Balneotherapie. Schlayer, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 544; Klin. Wchnschr. (Berl.), 1922, **1**, 970.

Diseases of the **pineal, parathyroids, hypophysis, adrenals** and **thyroid** cannot be treated by balneotherapy except in light cases, especially of Addison's disease, tetanoid attacks, etc. A good climate is often effective in slight cases of hyperthyroidism, chlorosis and osteomalacia.—J. K.

(ENDOCRINE ORGANS) Fetal chondrodystrophia in a calf (Zur Frage der Chondrodystrophia fetalis beim Kalbe). Seifried, München. med. Wchnschr., 1922, **69**, 417.

In this case of fetal chondrodystrophia in a calf the **hypophysis** was normal but all other **endocrine glands** histologically showed a defective development. In the **thymus** the cortex, when compared with the medulla, was abnormally large; the Hassall's corpuscles were very small and their number was diminished. The number of eosinophil and plasma cells in the thymus was also very small. According to Schridde this would prove a defective secretion of the organ.—J. K.

Influence of ENDOCRINE GLANDS on the sensibility to spasms (Weitere tierexperimentelle Untersuchungen über den Einflusz endokriner Drüsen auf die Krampffähigkeit). Specht, Klin. Wchnschr. (Berl.), 1922, **1**, 811; 1128.

A short note. The removal of the **thyroid, testicle** or **adrenals** has no influence on the sensibility of the animal to spasms.

—J. K.

Progressive LIPODYSTROPHY. Strauch (A.), J. Am. M. Ass. (Chicago), 1922, **78**, 1037-1038.

A case of this rare condition is reported and the various theories of its etology, including endocrinopathies, are discussed.

—W. M. A.

(ENDOCRINE GLANDS) Essential itching as a clinical symptom of pluriglandular insufficiency (Das essentielle Hautjucken als klinisches Symptom der multiplen Blutdrüsenerkrankung).

Szondi (L.) & Haas (L.), München. med. Wchnschr., 1922, **69**, 584-585.

Ten cases of pruritus are described in which no cause of the itching was found. In 6 cases there was a typical pluriglandular insufficiency. The 4 other patients also showed endocrine symptoms. One patient had **exophthalmic goiter**, positive Grafe symptom, and Neisserian oöphoritis. A second patient had a small **thyroid** with hard nodules. A third had **dysmenorrhea**, no sexual desires and a hypoplastic thyroid. The fourth showed only a hypoplastic thyroid and a want of sexual desires. Itching may be an extremely disagreeable symptom of an endocrine dysfunction. The author suggests that it may be explained by a hyperirritability of the sensitive nerves caused by toxic products of metabolism. This hyperirritability becomes itching in places that undergo regular irritation. **Organotherapy** gave only temporary relief.—J. K.

(ENDOCRINE ORGANS) Influence of organotherapeutic preparations on carbohydrate tolerance (Contributo allo studio della influenza dei prodotti opoterapici sulla tolleranza degli idrati di carbonio). Travaglini (V.), Gazz. d. osp. (Milano), 1922, **42**, 1200.

The pluriglandular theory of diabetes is the most probable. Therefore, polyphagia, polydipsia, tachycardia with inclination towards arhythmia are symptoms of an increased function of the sympathic system and may perhaps be due to hyperadrenalism. Though opotherapy does not cure diabetes, in some cases it may have some effect. In cases of typical pancreatic diabetes, injections of extract of pancreas (or extract of almonds which, as Farmachidis has shown, has the same influence) may have some influence on metabolism. The author believes that muscular exercise, ingestion of yeast, thyroid, opium, liver preparations and antipyretic drugs are all sometimes useful.—J. K.

ENDOCRINES and sympathetic. Vercellini (G.), Minnesota Med. (St. Paul), 1922, **5**, 211-216.

A general philosophic review.—R. G. H.

(GONADS) The ENDOCRINE functions of the female reproductive organs. Vincent (S.), Lancet (Lond.), 1922, **ii**, 303-305.

An excellent brief review of our present knowledge of the subject, including discussions on the effects of extirpation of the ovaries at various ages, in man and also in the lower animals; the transplantation of the ovaries; extirpation of the **corpus luteum**; and the relation of the corpus luteum to the gravid uterus. The article (which is an abstract of the Ingleby lectures delivered at the University of Birmingham in 1921) is conservatively written, as may be judged from this sentence in the opening paragraph: "A biologist has only to discover a group of cells whose function is not clear

and it is instantly charged with that of internal secretion; a medical man need only find some baffling symptom or syndrome, and forthwith the magical word 'hormone' relieves him of all further responsibility for investigation."—E. N.

Correlation of the ENDOCRINE glands (Korrelation der Blutdrüsen). Wagner (R.), Wien. klin. Wchnschr., 1922, **35**, 352.

A girl of 10 months had a tumor of the liver and a most remarkable disturbance of **carbohydrate metabolism.** On an empty stomach there was scarcely any blood sugar; after the ingestion of carbohydrates an enormous hyperglycemia was seen. **Adrenalin** did not produce a rise of the blood sugar. **Thyroidin,** when given repeatedly, produced hyperglycemia, lipemia and lipuria. A fat free diet produced an xerosis of both eyes. The author believes the disease to be a hepatogenous azooamylia (Naunyn) with hypothyroidism. —J. K.

Correlation of the ENDOCRINE glands. Wagner (R.) & Parnas (J. K.), Med. Klin. (Berl.), 1922, **18**, 137.

The girl of 10 seemed to have chronic interstitial hepatitis; the liver was very much enlarged, and in addition there was an odor of acetone about her when fasting, and there is glycosuria after ingestion of starch and sugar, but no sugar is found in the blood, fasting, although ketone bodies abound. After eating sugar and starch, the acetone disappeared, but intense glycosuria followed. This same sequence occurred day after day. Under **thyroid** treatment, lipemia, lipuria and steatorrhea developed. Wagner and Parnas theorize that the main disturbance in this case is the lack of the ability to form and store glycogen in the liver. In some respects the condition is like that of a mild **diabetes,** but it differs materially from the latter when sugar is not being supplied from without. There is no formation of sugar from the body reserves. But this takes place when thyroid treatment is given. This seems to suggest that the thyroid is in control of this function. They theorize further that the **pancreas** presides over the sugar metabolism; through the **liver** it checks the mobilization of glycogen; through the thyroid it influences the formation of sugar anew. The removal of the pancreas thus removes the brake on both these functions, and complete experimental diabetes is the result.—J. Am. M. Ass., **78**, 1174.

The importance of ENDOCRINOLOGY in normal and pathological physiology (Die Ergebnisse der Lehre von der inneren Sekretion für die normale und pathologische Physiologie). Weil (A.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 559-562.

A short but excellent review without new data.—J. K.

Constitution and ENDOCRINE ORGANS (Konstitution und endokrines System). Wuth (O.), München. med. Wchnschr., 1922, **69**, 392-394.

A general review without new data. The author states the importance of the endocrine organs to the physical and psychical constitution. Especially in psychiatry should more attention be given to these organs.—J. K.

Tuberculosis and glands of INTERNAL SECRETION (Tuberculosi e ghiandole a secrezione interna). Zibordi (D.), Riforma med. (Napoli), 1922, **38**, 295-298.

The author reports his experiments on guinea pigs in regard to tuberculous infection after removal of the **thyroid**, of the genital glands, and of the thyroid and genital glands. The removal of the thyroid alone did not cause any difference in the spreading of the infection; the removal of the **testis** did not sensibly slow the process. The removal of both testis and thyroid and **ovary** and thyroid, while not modifying the process in males, succeeded in rendering very slow and torpid the process of infection in females. The removal of ovary only showed a slight slowing of the process. A discussion follows on the presumed opposite action of the male and of the female genital gland on the thyroid, which would bring about hypofunction in males and hyperfunction in females.

—G. V.

Treatment of ENDOCRINE adiposity (Behandlung der endokrinen Fettsucht). Zondek (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 999-1000.

A good general review without new facts.—J. K.

ENDOCRINE adiposity (Ueber endokrine Fettsucht). Zondek (H.) & Loewy (A.), München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

In **hypophyseal** adiposity basal **metabolism** is not diminished. In cases of local adiposity, as they may be seen in light endocrine disturbances (**castration, pregnancy, Graves' disease,** etc.) a high, though not abnormaliy high, quantity of oxygen is used; but in one case of adiposity with Graves' disease enormous quantities were used. In these cases thyroid therapy had no effect. In ordinary cases of endocrine adiposity, however, thyroidin is very active. Thyroid preparations in which the proteins have been decomposed, such as **thyreoglandol** or **thyroidopton,** are absolutely inactive in endocrine adiposity.—J. K.

Development of human germ cells, etc. (Über die Bildung der menschlichen Geschlechtszellen und die Vorgeschichte der menschlichen Leibesentwicklung). Friedenthal (H.), Arch. f. Rassen-u. Gesellsch.-Biol. (Liepz. & Berl.), 1921, **13**, 257-276.

Not of endocrine interest.—A. T. R.

(OVARY) The oestrous cycle in the mouse. Allen (E.), Am. J. Anat. (Phila.), 1922, **30**, 297-371.

A study based upon more than ninety mice. It was found that external signs are unreliable criteria of oestrous in mice. The presence of cornified cells in the vaginal smear is a much more accurate indication. When these cells appear in masses, ovulation has usually occurred. Characteristic changes in vaginal and uterine epithelium are described. These are accompanied by periodic extrusion of nuclei from the epithelial cells of the oviduct. Ovulation is not always spontaneous in virgin or unmated mice. It is held that the corpora lutea have no primary causative relation to oestrous changes in the genital tract. The conclusion is drawn that the presence of maturing ova in large follicles is the cause of prooestrum and oestrus, and that the removal of the ova at ovulation (or their atresia if this fails to occur) is the primary cause of the degenerative changes of the metoestrum.—W. J. A.

(GONADS) Pseudo-hermaphroditism in male Cetacea (Le pseudo-hermaphrodisme tubaire chez les Cétacés mâles). Anthony (R.), Compt. rend. Acad. d. sc. (Par.), 1920, **171**, 1398-1399.

The almost constant occurrence of a greatly developed utriculous masculinus in some species of male Cetacea coincides in general with the poorly defined secondary sexual characteristics, and possibly with the absence of interstitial tissue in the testes, although only a single testis has been examined. The author names other orders in which there is regularly a persistence in the male of a considerable part of the Müllerian ducts.—A. T. R.

INTERNAL SECRETION of the OVARY (Sur la sécrétion interne de l'ovaire). Athias (M.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 296-306; abst. Physiol. Abst., **7**, 52.

A critical dissertation in which it is concluded that it is impossible at the present time to determine with certainty the specific parts of the ovary which function in producing specific hormones.—R. G. H.

(GONADS) Observations on the normal and pathological histology of the interstitial cells of man and mammals (Bemerkungen zur normalen and pathologischen Histologie der Zwischenzellen des Menschen und der Säugetiere). Benda (C.), Arch f. Frauenk. u. Eugenik (Leipz.), 1921, **7**, 30-40.

There is first given a general yet concise statement of the development, structure and significance of the interstitial cells (i. c.) of the gonads but more particularly of the testic. The origin is mesenchymal, in the opinion of the author. As a rule, but not invariably, degeneration of the tubules of the testis is accompanied by an increase in the interstitial cells. In syphilitic lesions of the

testis he found no interstitial cells, but between the necrotic areas were functional tubules and fairly large groups of these cells. They are fairly numerous in cachexia. In inguinal retained testes there are usually very few, while in typical cryptorchism they are most often greatly increased. In hermaphrodism, the interstitial cells are mostly found in the testicular part of the ovatestis. In a recently reported case of typical virilism there were none. In another case (masculine externally except for well developed mammary glands) the author found many interstitial cells in the testicular portion while the ovarian part contained a distinct corpus luteum. Older cases are similarly reviewed. A case is given of a 19 year old external masculine pseudohermaphrodite (feminine in appearance) from whom one of the two testes was removed. This contained typical testicular tissue, some portions of which were either infantile or contained degenerating and adenomatous tubules; but between the tubules of the pathological areas were large groups of typical interstitial cells. None were found in the ovary of a newborn feminine hermaphrodite. Four cases of homosexuality are detailed but there were no distinctive features.

In a case of Basedow's disease the interstitial cells were numerous and rich in fat. In a case of acromegalia there appeared to be regressive metamorphosis of these cells and some degeneration in the tubules. In a case of infantilism in a 20 year old man in whom the testes were not apparently infantile, there were only a few interstitial cells that were at all typical and these lacked fatty droplets. The testes of a 38 year old man with a teratoma in the sella turcica and great reduction of the hypophysis were infantile as to germinal epithelium and not a single typical interstitial cell could be found. Most of the descriptions are from personal observations. Benda concludes that while the normal and pathological anatomy of the interstitial cells of the testis undoubtedly contain many interesting problems, up to the present time no general uniformity as to their meaning is obtainable from the morphological data. Only a few references are given.—A. T. R.

(GONADS) The puberty gland (Die Pubertätsdrüse). Berberich, München. med. Wchnschr., 1922, **69**, 331.

The author believes that the interstitial cells have an unknown endocrine function. The sexual-endocrine function depends upon the spermatogenous cells. No details or reason are given.—J. K.

(TESTES) Operative attempts at organic rejuvenation or treatment of genitoglandular dystrophy (Os ensaios operatorios de rejuvenescimento organico e a therapeutica da dystrophia genito-glandular). Castro (A. de.), Prensa Méd. Argentina (Bs. Aires), 1922, **8**, 289.

An excellently presented discussion. Testicle grafting is indicated for three purposes: to rejuvenate; to ameliorate the symptoms

of castration; or to lessen the manifestations of genitoglandular dystrophy. In the second case the indication is simply the replacing of a missing organ. In the third case testicle grafting is merely the best resource available. Observations on three cases of eunuchoidism are reported.—B. A. H.

(GONADS) Relations between MENSTRUATION and different organs (Wechselbeziehungen der Menstruation zu den einzelmen Organen). Daude, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 544.

Of no endocrine interest.—J. K.

The SEX character as pathogenic factor (Könskaraktärens patogenetiska betydelse). Ehrström (R.), Finska Läk-sällsk. handl. (Helsingfors), 1921, **63**, 1-15.

In a preceding paper the author pointed out that there is a difference in frequency of "nephrosclerosis" in the two sexes. No such difference occurs in "nephritis" and "nephrosis." Stimulated by these findings the author has made a study of the literature concerning the relative frequency of different diseases in the sexes. He comes to the conclusion that the exogenic factors very often do not sufficiently explain this difference. There must be a variation of disposition and resistance due to the sex. A combination of exogenic factors and disposition is sometimes to be seen. The relation between man and woman as regards sporadic struma is 4:1; endemic struma, 2:1. Thus the exogenic factors in the endemic are strong enough to impress also the individuals with greater resistance. The sexual factors are of very great importance and those who try to reduce the difference between man and woman to a minimum are all false prophets.—H. B.

Development of a myoma after transplantation of an OVARY (Myomentwicklung nach Ovarientransplantation). Fleischmann C.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 82-83; Klin. Wchnschr. (Berl.), 1922, **1**, 348; München. med. Wchnschr., 1922, **69**, 101.

One woman suffered from amenorrhea and sterility, another from myoma of the uterus. Half of each of the two ovaries were transplanted. One ovary contained a small cyst, the other a corpus luteum. In the patient with amenorrhea the uterus enlarged after the operation, then a myoma developed, and menstruation, which the patient had not had for 16 years, returned.—J. K.

(GONADS) The problem of homosexuality (Das Problem der Homosexualität). Gaupp (R.), Klin. Wchnschr. (Berl.), 1922, **1**, 1033-1038.

A general review without new data.—J. K.

A case of TESTICLE transplantation with control after three months (Ein Fäll von Hodentransplantation mit Kontrolle nach einem Vierteljahr). Förster (W.), München, med. Wchnschr., 1921, **68**, 106-107.

A man of 55 with precocious senility was troubled with lymphosarcoma of the neck. When he was cured with x-rays a testicle, taken from a man of 20 years with cryptorchism, was implanted into the abdominal wall. The operation had no effect on the senility and the man died 3 months afterwards from cachexia. Necropsy disclosed complete necrosis of the graft.—J. K.

Absence of CORPORA LUTEA in a case of atypical uterine hemorrhage. Geist (S. H.), J. Am. M. Ass. (Chicago), 1922, **78**, 1185-1186.

A married woman of 28, mother of four children, had periods of several months' duration of alternating **amenorrhea** and **menorrhagia.** Examination of the tissues removed at operation revealed no pathological alterations sufficient to account for the condition except the absence of corpora lutea. The relation of the ovary to menstruation and pathologic bleeding is discussed. The conditions underlying the periods of amenorrhea are not considered.

—W. M. A.

(GONADS) Sex intergradation (Untersuchungen über Intersexualität). Goldschmidt (R.), Ztschr. f. indukt. Abstammungs-u. Vererbungsl. (Berl.), 1920, **23**, 1-199.

A highly technical discussion abstracted at length in Ber. ü. d. ges. Physiol., 1922, **11**, 467-471.—R. G. H.

Numerical analysis of the OVARIES of a healthy woman of 22. (Zahlenmässige Analyse der Ovarien eines 22 jährigen gesunden Weibes). Häggström (P.), Upsala Läkaref. Förh., 1921, **26**, 1-52; J. Aug. Hammar. Festskrift. Each article is paged separately.

The ovaries of an unmarried, healthy woman 22 years old who suddenly died of CO-intoxication were cut in sections 36 μ thick. Every 10th section was magnified 1:17 in the drawings. The borders of the sections, of the different parenchyma zones and of all the follicles, corpora atretica, lutea and albicantia being over 100 μ in size were indicated. The follicles were followed from section to section. The small follicles were drawn at a magnification of 1:200 in every 50th section. By measuring and counting the author obtained figures indicating the relation between the different parenchyma components and the absolute number of the follicles, the corpora lutea and atresia over 100 μ in size and finally the approximate number of the small follicles. The number of follicles was approximately 17,000 in the smallest and 250,000 in the largest ovary. The small follicles were most numerous; only

219 were over 100 μ in size. The values did not differ considerably when only every 100th section was counted. Of the follicles only 5 per 10,000 showed liquor folliculi. Two nuclei in one egg were found in every 416th follicle. The author points out that this figure agrees very well with the frequency of twins. Follicles with two ova were found only 5 times. The total number of the corpora atretica was approximately 12,000, most of them (9,000) being small. The percentage of corpora atretica of the small follicles was low (2%). On the other hand, the corpora atretica over 100 μ in size were 10 times as common as the intact follicles of the same size. The zona pellucida seems to be the most resistent component of the parenchyma and was found in every 4th of the corpora atretica. The number of corpora lutea was 9, 4 in one and 5 in the other ovary. The microscopic picture indicated that probably the bursting of the follicles had occurred alternately in the two ovaries. There were 48 corpora albicantia in the large ovary and 10 in the small one. Thus the follicles did not always burst alternately. The total number of corpora lutea and albicantia proves that the woman had menstruated at least 5 years before her death.—H. B.

Alimentary GLYCOSURIA as a diagnostic test (Die Alimenfäre Glycosurie als diagnostische Probe). Hofbauer (J.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 348-351.

Many years ago the author proved that alimentary glycosuria was a rather reliable diagnostic test for pregnancy. It was positive from the end of the second month; later on, during pregnancy, it might become negative again. These observations have been confirmed by newer studies of Frank and Nothmann and of Nürnberger. Hofbauer believes that the placenta stimulates the hypophysis and the **thyroid** and that therefore it is possible to consider this test as a test for the presence of a normally functioning placenta. Perhaps the disturbed function of the liver also plays a role in this test. It is remarkable that the ingestion of 200-300 gm. will, in pregnancy, produce a "crise haemoclascique."—J. K.

(OVARY) Observations on the sexual cycle of the white rat. Ishii (O.), Anat. Record (Phila.), 1922, **23**, 311-314.

The author presents a summary of the outstanding features of his studies on the oestrous cycle. In certain points he differs from other recent authors. The first oestrous appears, according to Ishii, at an age of 32 to 40 days. The period of heat is distinguished as a shorter part of general oestrous, generally occurring at night. He denies that sterile copulation lengthens subsequent oestrous periods.
—W. J. A.

ENDOCRINE aspect of female sterility. Jacoby (A.), Med. Rec. (N. Y.), 1922, **101**, 239-241.

The author reviews briefly the physiology of the uterus and ovaries, and urges that every case of sterility in which gross pathological conditions can be excluded warrants a careful study of the individual with a view to determining any malfunction of the endocrine system and the use of the indicated extracts for prolonged periods. He cites two cases which he believes illustrate the value of **organotherapy** in sterility under certain conditions. The first patient he believes to have suffered from deficient ovarian secretion. She had been married two years, without pregnancies. The administration of 5 grains of **ovarian extract** three times a day for two months was followed by pregnancy. In the second case, which the author thinks was one of deficient development of the **ovary** plus a diminished activity of the **pituitary,** he attributes the good results to the administration of ovarian extract in similar dosage, in addition to one-half mg. of pituitrin, hypodermically, three times a week.

E. N.

(GONADS) Certain cases of hermaphroditism, with special reference to the interstitial cells (Über einige Fälle von Hermaphroditismus, mit besonderer Berücksichtigung der Zwischenzellen). Keussler H. von), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67,** 416-436.

Three subjects of hermaphroditism with female secondary characters, possessed **testes** with interstitial cells. The author interprets his observations as opposed to Steinach's theory of the **"puberty-gland."**—W. J. A.

(GONADS) The reproductive glands and mental disorder with special reference to dementia praecox. Kirby (B. H.) & Gibbs (C. E.), State Hosp. Bull. (Utica), 1921, **6,** 147-158.

An interesting general discussion is followed by a record of the size and consistency of the testes in 313 psychotics as determined by palpation. Random (alphabetical) selection of subjects was employed. The results are indicated in the subjoined table.

Variations in Size and Consistency of the Testes

	Number of cases	Abnormal size, per cent	Abnormal consistency, per cent	Abnormal size and consistency, per cent
Dementia praecox.....	186	56	47	31
Manic-depressive	50	46	22	12
General paralysis.....	49	42	58	28
	285			

Columns showing abnormal size and abnormal consistency include cases showing both changes in the same individual as shown in last column. The unusually favorable situation of State Hospitals for post-mortem endocrine studies is emphasized.

—R. G. H.

(GONADS) Ovariotestes in the goat (Ovariotestes bei der Ziege). Krediet (G.), Biol. Zentralbl. (Leipz.), 1921, **41**, 447-455.

Hermaphroditism is fairly common in goats. Most cases are, however, pseudohermaphroditic. Of the twenty cases observed by the author in which the genitalia appeared feminine but the head and general habitus masculine, only three are taken up in detail. Two of these had gonads which contained both testicular and ovarian structures, but there were no typical ovarian stroma cells which could be called a female "puberty gland" (unless this was represented by theca interna cells or other elements); and yet the animal showed some female characteristics (e. g., gave considerable milk). In a third goat, 4 months old, there were no interstitial cells clearly recognized in the ovariotestes. The significance of such close association of male and female gonadal elements with reference to the Steinach's theories, mono- and bi-sexuality and to Lillie's theory of the cause of freemartins is discussed. The histological findings in the hypophysis of only one of the three goats is briefly stated. No references.—A. T. R.

(GONADS) Transplantation of testicle and homosexuality (Hodentransplantation und Homosexualität). Kreuter (E.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 548-550.

Some years ago (see Endocrinol. 1920, **4**, 318) the author described the use of testicle transplantation after castration. He has now completely changed his opinion because the grafts nearly always become necrotic. In a previously normal patient who had been castrated on account of tuberculosis he grafted a testicle of a homosexual man. After the transplantation the patient sometimes had erections and his feelings remained heterosexual without the slightest trace of homosexuality. The effect of the transplantation on the physical symptoms of the castration was nil.—J. K.

(GONADS) Pregnancy and menstruation glycosuria (Schwangerschafts und Menstruationsglykosurie). Küstner (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 312.

It is well known that during the beginning of pregnancy the tolerance for sugar may be low. The author tried to determine whether this was due to the ovum. He found, however, that women sometimes have sugar in the urine even when the blood sugar is no more than 0.13 to 0.18 per cent. This occurs a few days before menstruation. It is probable that some relationship exists between pregnancy (and menstruation), glycosuria and the ovary.—J. K.

(GONADS) Development of the interstitial glands (Zur Entwicklung der interstitiellen Geschlechtsdrüse). Lahm, Klin. Wchnschr. (Berl.), 1922, **1**, 299. See also München. med. Wchnschr., 1922, **69**, 485.

The interstitial cells have a trophic function. In the testicle they arise from the epithelium. The secondary sexual characteristics depend upon the seminal cells.—J. K.

(TESTES) The significance of the thymus in the development of the male sex glands (Die Bedeutung des Thymus für die Entwicklung der männlichen Keimdrüsen). Leupold (E.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67**, 472-491.

The conclusion is reached that the testis is dependent, for its normal development, upon the combined influence of the thymus and the adrenal. It is held that the influence of the thymus upon the testis is through an effect upon the adrenal.—W. J. A.

GONADS and growth (Glandes génitales et croissance). Lereboullet (M.), Progrès méd. (Par.), 1922, **37**, 137-140.

A lecture discussing in a general way the relation of the gonads to growth.—R. G. H.

New observations on the endocrine function of the interstitial cells of the mammalian TESTICLE (Nouvelles observations sur la fonction endocrine des cellules interstitielles du testicule chez les mammifères). Lipschütz (A.) & Wagner (C.), Compt. rend. Soc. de biol. (Paris), 1922, **86**, 306-307.

The theory of the endocrine function of the interstitial cells of the testicle has been attacked of late on the ground that eunuchoidism is possible even in their presence, the generative tissue accomplishing the endocrine function. In studying compensatory hypertrophy of the testicle after unilateral castration, it was observed that in animals castrated at about six weeks of age the penis was still infantile at six and a half months, while the testicles remaining weighed 85 per cent more than controls from the same litter. The tail of the epididymis was full of living spermatozoa. Somatic eunuchoidism is thus possible in the presence of complete spermatogenesis. In these eunuchs the interstitial cells showed marked differences. The nuclei were small, the protoplasm less abundant. In some places the cells were better developed. These observations demonstrate that well developed interstitial cells are a necessary condition for the endocrine function of the testicle.—T. C. B.

(GONADS) The minimum amount of TESTICULAR substance necessary for the attainment of normal sexual character (Ueber das minimum der Hodensubstance, das für der Geschlechtsmerkmale ausreichend ist). Lipschütz (A.), Ottow (B.) & Wagner (K.), Arch. f. d. ges. Physiol. (Berl.), 1921, **188**, 76-86.

If 1% of the total testicular substance of a male guinea pig is left within the animal it suffices for the development of the normal somatic sexual characteristics. When 0.5% or less remains the ap-

pearance of the signs of total castration are retarded. In testicular tissue there may occur a complete degeneration of the spermatogenic tissue after section of vas deferens, x-radiation or transplantation. If partial castration is done before sexual maturity, spermatazoal ripening may occur. The interstitial cells in a well vascularized testicular residue are markedly increased in number.

—F. S. H.

Interstitial cells in guinea-pig TESTIS. Lipschütz (A.), Ottow (B.), Wagner (C.), & Bormann (F.), Proc. Roy. Soc. (Lond.), 1922, **93 B,** 132-142.

Hypertrophy of these cells is not compensatory, and it does not always occur after castration. Whether it occurs is due to local conditions, the most important factor being blood supply. The hypertrophy occurs markedly in the upper portion of the testis, which is better supplied with blood than the lower part.—

—Physiol. Abst.

(GONADS) A case of true lateral hermaphroditism in man (Ein Fall von Hermaphroditismus verus lateralis beim Menschen). Losert (J.), Beitr. z. klin. Chir. (Tübing.), 1921, **122,** 411-417.

A 19 year old soldier was operated upon for inguinal hernia and cryptorchism. Near the left inner inguinal ring was a 3x2.5x2 cm. **ovary;** histologically it was essentially like that of a sexually mature woman. It contained **corpora lutea** and follicles in all phases. A small uterus and attached tube were also removed. A careful description of these structures and related ligaments is given. The left scrotal sac was empty, but the right contained a **testis** 2.5 cm. in diameter with palpable epididymis and ductus deferens, from which a milky fluid could be obtained. While spermatozoa were not found it appeared certain that there was a right testis. The reactions of Florence and Barberio were negative. The individual in general appeared and acted masculine and had fairly well developed external male genitalia; but there were some female characteristics, especially the well developed mammary glands, which commenced to enlarge at the age of 13. There were no indications of any menstrual periods. Observations 1½ years after the removal of the ovary showed that there had been no increase in the size of the penis or in libido; but the mammary glands had decreased noticeably and were distinctly more flaccid. Comparisons are made with six other cases on record, but no specific references to literature are given.—A. T. R.

(GONADS) Hermaphroditism (Über Hermaphroditismus). Mittasch (G.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67,** 142-180.

A case of pseudo-hermaphroditismus masculinus internus in an individual 54 years of age. A rather comprehensive review of simi-

lar cases in the literature is given and the theoretical considerations are discussed.—W. J. A.

"All or none" law or the functional constant relative to the action of the TESTICLE as an endocrine gland (Loi du "tout ou rien" ou de constance fonctionnelle, relative à l'action du testicule considéré comme glande endocrine). Pézard (A.), Compt. rend. Acad. de sc. (Par.), 1921, **172**, 89-92.

Subperitoneal grafting of portions of testis in castrated cocks leads to the development of secondary sexual characteristics if the weight of testis implanted is 0.5 gm. or more. If the graft has a lower weight than this, the animal remains neuter. There is no intermediate state.—Physiol. Abst., **6**, 75.

Latent period in the experiments of TESTICULAR transplantation and the "all or none" law (Temps de latence dans les expériences de transplantation testiculáire et loi du "tout ou rien"). Pézard (A.), Compt. rend. Acad. de sc. (Par.), 1921, **172**, 176-178.

After grafting testicular tissue in castrated cocks there is a latent period of 2 to 6 weeks, during which there is no difference between the animals and control cocks, which have been castrated without implantation of testicular tissue. Then comes a sudden divergence, and the grafted animals develop secondary sexual characteristics at a rapid rate.—Physiol. Abst., **6**, 76.

(GONADS) A cured case of homosexuality, treated by transplantation of a testicle (Ein geheilter Fall von Homosexualität durch Hodentransplantation). Pfeiffer (E.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 660-662.

The patient was a man of 33. From his twenty-first to his thirtieth year no abnormal sexual desires were experienced. Then he dreamed of men and felt sexual excitement when in the presence of men. The pubic crines were of somewhat feminine type. The patient was operated upon for hernia and, unknown to him, a piece of testicle was ingrafted. Some weeks later the pubic scutcheon had increased in size and the patient not only had normal sexual desires but wished to marry.—J. K.

Interstitial cell tumors of the TESTIS in bird hybrids (Zwischenzellengeschwülste des Hodens bei Vogelmischlingen). Poll (H.), (Beitr. z. path. Anat. u. z. allg. Path. (Jena.), 1920, **67**, 40-56.

Hybrids produced by crossing the peacock and the guinea fowl exhibit a great development of interstitial cells amounting almost to tumor-like growths.—W. J. A.

(OVARY) Some aspects of vascular hypertonus. Ritchie (H. J.), M. J. Australia (Sydney), 1922, **1**, 318-322.

"The only type of hypertension in which endocrine imbalance has been proved to play a part is that met with in women about the climacteric, which often yields rapidly to the administration of extract of **corpus luteum.**"—Quoted.

(GONADS) Spermatogenic or interstitial cells (Geschlechtszellen oder Zwischenzellen). Romeis (B.), Klin. Wchnschr. (Berl.), **1,** 960-964; 1005-1010; 1064-1067.

This is the best of the many reviews on this subject. No new facts are given. According to the author, there is no valuable proof that the interstitial cells have an endocrine function. The problem of the interstitial cells still exists. Though it cannot be denied that these cells have a trophic function, it is not improbable that they still have other functions.—J. K.

The role of the lutein cells of the OVARY in certain uterine hemorrhages (Du role des cellules lutéiniques de l'ovaire dans certaines hémorrhagies utérines). de Rouville (G.) & Sappey (P.), Gynéc. et Obstét. (Par.), 1922, **5,** 1-38.

The basis of this contribution is the histological study of 6 cases in which uterine hemorrhage was present, as compared with 6 in which there was no hemorrhagic tendency. The authors believe that **menstruation** is produced by an internal secretion of the lutein cells, either the so-called interstitial cells of the theca interra of atretic follicles or the lutein cells of the corpus luteum. They conclude, from the study of this small series, that hyperfunction of these cells produces pathologic uterine bleeding, that an average or normal function produces normal menstruation, and that a hypofunction of these cells entails amenorrhea. They emphasize that in the interpretation of the secretory capacity of these cells, the macroscopic appearance of the ovaries, whether they be cystic or not, is of no significance. Microscopic examination alone can give accurate information.—E. N.

(GONADS) The present view on Steinach's rejuvenation (Der gegenwärtige Stand der Steinachschen Regenerationslehre). Schmidt (P.), Ztschr. f. ärztl. Fortbild. (Jena), 1922, **19,** 14-17.

A short general review. The author saw cases in which ligation of the vas deferens gave good results. No result may be expected, however, when the testicles of the patient show a marked senile atrophy. No case reports are given.—J. K.

(TESTES) Internal secretion and Steinach's rejuvenation (Innere Sekretion und das Steinachsche Verjüngungsproblem). Schmidtgen & Gruber, München. med. Wchnschr., 1922, **69,** 98.

A short general review without new data.—J. K.

The toxicity of PLACENTA lipoids. Schönfeld (H. E. H.), Arch. f. Gynæk. (Berl.), 1921, **115**, 80-125.

From the normal placenta various toxic substances may be isolated. Alcohol, acetone and glycerol extracts contain two substances which are insoluble in ether or petroleum ether. One substance produces convulsions in mice when injected subcutaneously. This substance is thermolabile, is activated by glycerol and is probably of the nature of an enzyme. In the same fraction there is a more thermolabile substance which causes uterine contractions. In extracts made with alcohol, ether, chloroform or other lipoid solvents there are also 2 toxic substances, probably lipoids. One causes the formation of thrombin, particularly in the lungs and liver. The other substance is toxic for liver, kidney and endothelial cells. Several of these factors may play a role in the causation of eclampsia. The lipoid content of the blood is high in the latter half of pregnancy and particularly high in eclampsia. At the slightest indication of eclamptic symptoms a detection of the lipoid content of the blood would be of diagnostic value. Eclampsia may be considered as the result of an abnormal internal secretion of the placenta, with an accumulation of the secretion in the blood through lack of elimination through the liver or insufficient neutralization by other antagonistic endocrine substances, particularly the **corpus luteum.**

—Chem. Abst., **16**, 1272.

The terminology of MENSTRUAL disorders (Über die Benennung der Menstruationsunregelmässigkeiten). Seitz (L.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 50-53.

An interesting nomenclature of menstrual irregularities, but not of especial endocrine interest.—E. N.

(GONADS) New investigations on the interstitial cells (Neue Untersuchungen über die Zwischenzellen). Stieve (H.), Verhandl. d. anat. Gesellsch. (Jena), 1921, **30**; Ergnzshfte z.; Anat. Anz., 1921, **54**, 63-76.

After an introductory definition of the "puberty gland," the enormous increase in the **testis** of Colaeus monedula collaris Drmd. (European jackdaw), from the sexually quiescent stage of January to that of the breeding stage in April is described. Volumetric determinations show this increase to be, in one particular case, 418 times. This is largely due to an increase in the germinal epithelium and not to interstitial tissue. The increase may be as great as 1,000 times. In the male domestic goose Stieve found that fattening modifies the secondary sex characters and interferes with the onset of the breeding period and these in turn apparently injure the germinal cells, which degenerate, and increase the amount of interstitial tissue. Absolute figures of the amount of the various tissue in the testes is given as well as the amount per gram of body weight.

The increase in interstitial tissue coincided with a loss of secondary sex characters and the production of sterility. This, the author thinks, rather indicates that the internal secretion generally attributed to the interstitial cells comes from the germinal epithelium in the case of the goose.—A. T. R.

(HISTAMINE) Imidazolylethylamine and organ extracts. I. β-Imidazolylethylamine as a powerful stimulant of the gastric glands. Popielski (L.), Arch. f. d. ges. Physiol. (Berl.), 1920, **178**, 214-236.

In addition to its other effects, histamine acts as a strong stimulant of gastric secretion. When injected subcutaneously into dogs in amounts of 0.00021 gm. per kgm. of body weight secretion of gastric juice, of normal acidity and pepsin content, follows. The secretion begins within 10 minutes, attains its maximum within 45-60 minutes, maintains a high level for an hour, and then gradually diminishes in amount. The total amount secreted is about 3.75 cc. per kgm. When administered by other routes the effects vary; oral introduction is without effect, and after intravenous injection the pancreatic, salivary, and lacrymal glands show increased activity. Section of the vagi, or the administration of atropine, does not essentially modify the secretory effect. It is suggested that the effective material in organ extracts which manifest the same properties is β-imidazolylethylamine.—Chem. Abst.

(HYPOPHYSIS) Clinical study of a case of ACROMEGALY. Benjamin (J. E.), J. Am. M. Ass. (Chicago), 1922, **78**, 499-501.

The case report of a young man is given in detail and is well illustrated with photographs and roentgengrams.—W. M. A.

Standardization of HYPOPHYSIS preparations (Wertbestimmung von Hypophysenpräparaten). Bijlsma, München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

A short note. To determine the therapeutic value of hypophysis preparations the **uterus** of a guinea pig is used. This method, however, gives an idea only of its obstetrical use and not of its activity in the treatment of **diabetes insipidus**.—J. K.

X-rays and tumors of the HYPOPHYSIS (Röntgenstrahlen und Hypophysentumoren). Biro, München. med. Wchnschr., 1922, **69**, 722.

A short note. Eight cases have been treated with large doses of x-rays. For over a year 6 of them have had no symptoms.—J. K.

X-ray treatment of tumors of the HYPOPHYSIS and of HYPOPHYSEAL gynecological diseases (Ueber Hypophysenbestrahlungen bei Hypophysentumoren und bei gynäkologischen Erkrankungen

hypophysären Ursprungs). Blumberg, München. med. Wchnschr., 1922, **69**, 739-741.

An exact description of the technical procedures in exposing the sella to the x-rays.—J. K.

Experimental contribution to the problem of HYPOPHYSEAL DIABETES (Experimentelle Beiträge zur Frage des hypophysären Diabetes). Brugsch (T.), Dresel (K.) & Lewy (F. H.), München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

The innervation of the hypophysis is not certainly known. Weed, Cushing and Jacobsen have found that innervation comes also from the plexus carotid and that stimulation of the superior cervical ganglia after section of the sympathic causes glucosuria. The authors could not confirm this; if the experiment as described by Cushing is carried out, the blood sugar is diminished. The existence of a hypophyseal diabetes has never been proved.—J. K.

(THYROID) Some aspects of exophthalmic goiter. Campbell (J. M. H.), Quart. J. Med. (Oxford), 1921, **15**, 55.

A study of the signs and symptoms, etiology, prognosis and distribution in England and Wales of 127 cases of exophthalmic goiter, treated at Guy's Hospital between 1908 and 1917. This study contains nothing new, but is of interest from a statistical viewpoint.—F. C. P.

Erythropoietic function of the HYPOPHYSIS (Erythropoïése dans l'hypophyse). Collin (R.) & Baudot (J.), Compt. rend. Soc. de biol. (Paris), 1922, **86**, 596-598.

Histological. It is thought that if the conditions described are found in other mammals than the guinea pig (the animal studied), we may conclude that the embryonic hypophysis has a hematopoietic function.—T. C. B.

Studies on the effect of diet on the weight of the HYPOPHYSIS and THYROID gland of the albino rat, and on the action of their extracts on the isolated small intestine. Degener (Lyda M.), Am. J. Physiol. (Balt.), 1922, **60**, 107-118.

This research was undertaken to determine the effect of different diets on the weight of the thyroid and hypophysis and on their extracts, using isolated intestine as an index. In one series three different diets were used; oatmeal, vegetables, and meat, respectively. In another, potassium, iodide and thyroxin were used in addition. Normal diet was fed to the controls. The body weights in all the groups were low, but the controls were heavier by about 5 gms. All the glandular weights were low for the body weights. The oatmeal thyroids were heavier than the controls by 1 mgm.;

the hypophysis, by 2 mgm. In the vegetable group the thyroid was heavier by 4 mgm., due to one unusually large male. In the meat group the thyroid was heavier; the hypophysis was not altered. As for the activity of the extracts, there seemed to be no difference between the thyroids of the test and of the control animals. In the oatmeal and vegetable groups the extract of the hypophysis caused contraction of the isolated intestinal strip. The control always caused relaxation. Extracts of the pars anterior caused contractions; of the pars nervosa, relaxation. It is suggested that in the results from oatmeal and vegetable diets the effect of the pars anterior predominates.—T. C. B.

The HYPOPHYSIS following brain lesions (L'ipofisi nelle lesioni del cervello). Desogus (V.), Riforma med. (Napoli), 1922, **38,** 329-330.

The author reports his observations on the hypophysis in experiments on dogs in which either both the cerebral hemispheres, or only the occipital or the parietal or the frontal lobe had been removed. The results were the same which ever part of the brain cortex was destroyed. In 20 to 30 days after the trauma, hyperfunction of the hypophysis was found with intense hyperemia, eosinophilia and secretion of pure eosinophil colloid (same as basophil in the parenervous lobe). In 30 to 60 days the eosinophils began to fade while the "chief" cells became evident. The capillary vessels were full of colloid, causing the organ to appear almost like a thyroid. The glandular parenchyma showed lacunae as if it were disintegrating. Analogous appearance was shown by the nervous portion and by the paranervous lobe, still basophil. From the 60th to the 90th day, eosinophils and basophils almost disappeared, while the chief cells were more evident than ever. The colloid became almost mother-of-pearl in color and was very abundant to the extent of breaking the capillaries and forming real colloid lakes. When the colloids had been absorbed the hypophysis showed a condition of absolute rest. After the 100th day there was a functional reintegration of the gland. The author recalls analogous results obtained by Ceni in the **thyroid** and **suprarenal** and the opposed results also obtained by Ceni in the male and female **sexual gland.** From this he infers the existence of a special viseral center on the brain cortex, connected with the function of the sexual and endocrine glands. The genetic centers have an exciting function. From the aforesaid, one can deduce that in dogs from one to two years old in which the animal regains normal condition after a brain cortex lesion in a period from 20 to 100 days, the hypophysis undergoes the following changes: hyperemia, secretion, hypersecretion, colloid resorption, rest of the organ and functional reactivation.—G. V.

(HYPOPHYSIS) Dystrophia adiposo-genitalis with muscular atrophy (Dystrophia adiposo-genitalis mit Muskelschwund). Fränkel (F.),

Deutsche med. Wchnschr. (Berl.), 1922, **48**, 373; Klin. Wchnschr. (Berl.), 1922, **1**, 549.

Demonstration of a patient who had been unable to walk since he was 8 years of age, and who always was extremely fat. He was 150 cm. in height and 100 kg. in weight. The hair was poorly developed; the generative organs were small; there was pseudoatrophy of the calves and atrophy of the glutei. His carbohydrate tolerance was low. The combination of dystrophia musculorum and hypoplasia of the hypophysis is not at all rare. It is probable that the endocrine organs have an influence in these diseases of the muscles.
—J. K.

Tumor of the HYPOPHYSIS improved by x-rays (Durch Röntgenbestrahlung gebesserter Fall von Hypophysistumor). von Gerlóczy (G.), Klin. Wchnschr. (Berl.), 1922, **1**, 1187.

A short note. The symptoms included almost complete amaurosis, large sella cessation of menstruation, headache, vomiting and giddiness. After x-ray treatment the eyesight was markedly improved and the symptoms of high intracranial pressure disappeared. In a case of hypophyseal **infantilism** x-ray treatment caused hypophyseal **cachexia.**—J. K.

Tumor of the HYPOPHYSIS. Goerke & Freund, Klin. Wchnschr. (Berl.), 1922, **1**, 297.

A man of 69 had had a loss of physical and intellectual forces for 3 years. The only symptoms of a tumor of the hypophysis were the bitemporal hemianopsia and a typical radiogram. He was given surgical treatment, but it is not told whether this was successful.
—J. K.

Influence of HYPOPHYSIS extracts on the alimentary tract and the blood of men (Einflusz von Hypophysenextrakten auf den Magen-Darmtraktus und das Blut des Menschen). Gorke (H.) & Deloch (E.), Arch. f. Verdauungskr. (Berl.), 1922, **29**, 149-163.

Subcutaneous injections of extract of neuro-hypophysis has the following effects. Secretion of salivary glands, **pancreas** and bile is diminished, but the ferment—or the bilirubin and cholesterin content is increased. The quantity of stomach content is generally increased; the acidity and the ferment content is diminished. Many persons show an increased tonus and peristalsis of the stomach and bowels. A few patients show an increased secretion of salt, bile and pancreatic juice and a low secretion of the stomach. Persons with an irritable nervous system show very strong reactions. In the blood a relative and absolute rise of leucocytes is seen. This is never very marked, however. The **blood sugar** does not show important changes.—J. K.

Tumor of the HYPOPHYSIS cured by radium (Ein Fall von Hypophysentumor geheilt durch Radium). Hirsch, Wien. klin. Wchnschr., 1922, **35**, 402; Klin. Wchnschr. (Berl.), 1922, **1**, 1237.

A short note. The optical symptoms disappeared very soon. —J. K.

Characteristic effects upon growth, oestrus and ovulation induced by the intraperitoneal administration of fresh anterior HYPOPHYSEAL substance. Evans (H. M.) & Long (J. A.), Proc. Nat. Acad. Sc. (Balt.), 1922, **8**, 38-39.

The authors have shown that rats treated intraperitoneally with fresh extracts of beef hypophysis (anterior lobe), show an acceleration of growth which is in marked contrast to the lack of effects from oral administration. In this paper they report two series of experiments with litter mate controls which have been under observation more than a year. The animals are invariably heavier than the controls. In one case a rat having received hypophyseal extract weighed 596 grams on the 333rd day of life, while its healthy litter mate control weighed 248 grams. There was a large deposition of fat, but also an increase in the size and weight of the skeleton and of the viscera. The hypophysis, **thyroid** and **thymus** were not appreciably affected. Oestrus may never occur in these animals, or may be exhibited only at long intervals, and it was surprising to find the **ovaries** twice as heavy as those of the controls, and containing great numbers of **corpora lutea.** The uterus weighed only half as much as that of the controls. Histologically there was abundance of lutein tissue and normal graafian follicles. Extracts of the posterior lobe gave no such effects.—T. C. B.

Composition of the urine and of the blood of dogs deprived of the HYPOPHYSIS (Composition de l'urine et du sang des chiens privés d'hypophyse). Houssay (B. A.) & Mazzocco (P.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 409-410.

Adult dogs were kept in metabolism cages and the observations extended over a month for each dog. Some had total extirpation of the hypophysis, some were operated upon without disturbing the gland, some had a fragment of gauze left behind the hypophysis, and finally some were kept as normal controls. The results show that the blood and urine are normal in dogs deprived of the hypophysis. Tables are given.—T. C. B.

(HYPOPHYSIS) Endocrinology of distrophia adiposo-genitalis. Kanai (T.), Nisshin Igaku, 1922, **11**, (No. 5); Jap. Med. World (Tokyo), 1922, **2**, 166.

The case was diagnosed by clinical symptoms. Pituitrin or pilocarpin gave negative results. According to the classifications of Eppinger and Hess it belonged to the sympathicotonic group

Marked glycosuria was brought on by administration of 50 gms. of glucose, or by giving **adrenalin.** Histidin prevented the glycosuria but cilosin and tryptophan had no controlling effect.—R. G. B.

Gas metabolism in diseases of the HYPOPHYSIS (Gaswechseluntersuchungen bei Hypophysenerkrankungen). Kestner, München. med. Wchnschr., 1922, **69,** 796; Klin. Wchnschr. (Berl.), 1922, **1,** 1280.

In dystrophia adiposo-genitalis, metabolism and the intake of food are only very slightly increased. Low metabolism is found in hypophyseal **nanism** and in some cases of endogenous **adiposity.** Injections of extract of pars anterior causes the metabolism to rise. —J. K.

The clinical pathology of the HYPOPHYSIS and the interbrain (Beiträge zur klinischen Pathologie der Hypophyse und des Zwischenhirns). Leschke (E.), München. med. Wchnschr., 1922, **69,** 796; Klin. Wchnschr. (Berl.), 1922, **1,** 1280.

The greatest quantity of active principle of hypophysis is found in the pars intermedia. **Uterus** contraction and a decreased diuresis are caused by different amins, resembling, but not identical with, histamin. Extract of pars anterior has an influence on **metabolism** useful in treatment of cachexia. Degeneration of the hypophysis causes **cachexia,** but never dystrophia adiposogenitalis or **diabetes insipidus.** Localization of these last mentioned diseases is in the interbrain, which, in turn, is influenced by the hypophysis. The hypophysis and interbrain have a regulating influence on each other. —J. K.

A case of HYPOPHYSEAL cachexia (Ein Fall Simondsscher Krankheit). Lichwitz, Klin. Wchnschr. (Berl.), 1922, **1,** 397-398; Deutsche med. Wchnschr. (Berl.), 1922, **48,** 500; München. med. Wchnschr., 1922, **69,** 138.

The disease began in an acute form, with **diabetes insipidus,** loss of flesh, loss of beard and other hair, sexual impotence, and hemianopsia. The skiagram of the sella showed enlargement with a calcium shadow. X-ray treatment and administration of hypophysis preparations had a splendid effect. The concentration power of the kidney for sodium chloride did not become normal, however.—J. K.

Genital dystrophy of HYPOPHYSEAL origin (Genitale Dystrophie hypophysaren Ursprungs). von Liebermann (L.), Klin. Wchnschr. (Berl.), 1922, **1,** 604.

A woman of 44 had a very small sella turcica, and a partial atrophy of the optic nerve. No other details are given.—J. K.

(HYPOPHYSIS) Independence of pulmonary circulation. McDowall (R. J. S.), Brit. Ass. Report, 1921, 446.

Pituitary extracts cause rise of pulmonary pressure (60 experiments, Sharpey Schafer's method), which has no relation to any changes in aortic pressure. Perfusion experiments with the surviving lung support the view of independence.

—Physiol. Abst., **7**, 34.

(HYPOPHYSIS) Dystrophia adiposo-genitalis. Meisner, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 647; Klin. Wchnschr. (Berl.), 1922, **1**, 497.

A girl of 15 years, 1.33 M. in height and 41.3 kg. in weight, was troubled with atrophy of the optic nerves and peripheral chorioretinitis. No bitemporal hemianopsia was apparent. The Wassermann test was negative. No other details are given.

—J. K.

The physiological assay of PITUITARY extracts. Nelson (E. E.), J. Pharmacol. & Exper. Therap. (Balt.), 1922, **19**, 270-271.

Ten commercial preparations of pituitary extracts were assayed. Some were ten times the strength of others. The pressor method is satisfactory for the comparison of a large number of preparations. The pressor activity, however, is not necessarily a measure of the oxytocic strength. The most satisfactory test for the latter is the virgin guinea-pig uterus. Histamine is unsatisfactory because it is unstable. Potassium chloride is unsatisfactory because the irritability of uteri toward pituitary extract and this does not vary in a parallel manner.—F. A. H.

(HYPOPHYSIS) Use of PITUITRIN in inoperable cancer. Norgate (J. H.), Brit. J. Surg. (Bristol), 1922, **9**, 495.

During a severe outbreak of enteric fever in 1919, finding that pituitary extract (posterior infundibular) controlled the hemorrhage cases without any bad symptoms, Norgate tried it in a case of sudden and severe hemorrhage from an extensive epithelioma of the tongue with enlarged cervical glands, injecting 1 cc. into the tongue muscle. All bleeding stopped at once, and there was no repetition of it. Weekly injections into the tongue were given for three months, and the patient made rapid improvement, put on flesh, and the cachexia disappeared. He continued nine months in the state; then a hard mass formed in his liver, the growth in the tongue remaining the same, the glands slightly enlarged, and he died very emaciated. The first injection was given May 12, 1919, and he died April 27, 1920. His melancholy and suicidal tendencies improved up to about a month before his death. Similar results were obtained in thirty-six other cases. No claim is made by Norgate that pituitary extract is a cure for cancer, for it only delays the growth by cutting off its blood supply for a limited time; but as a general tonic to the system, as a great antagonist to cachexia

and its attendant distress of mind and body, and as an agent in producing a remission for a time of the "last sentence" its value is great.—J. Am. M. Ass., **78**, 1760.

(HYPOPHYSIS) Operierter Hypophysistumor. Oehlecker, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 407.

A patient with dystrophia adiposo-genitalis suffered from severe headaches, disturbances of sight, vertigo, etc. After the operation there was improvement which lasted for about three years.

—J. K.

Tumor of the HYPOPHYSIS. Oehlecker & Fahr, Klin. Wchnschr. (Berl.), 1922, **1**, 299.; München med. Wchnschr., 1922, **69**, 29.

The patient was a woman of 31 with dystrophia adiposo-genitalis and bitemporal hemianopsia. A tumor was removed and she was cured for the time, but died two years later from recurrence. The tumor showed the picture of hypophysis tissue. No symptoms of hypophyseal cachexia had developed.—J. K.

(HYPOPHYSIS) GIGANTISM with hemorrhagic osteomyelitis of a metacarpal bone. Packard (M.) & Barrie (G.), J. Am. M. Ass. (Chicago), 1922, **78**, 8-10.

A case of so-called preadolescent hyperpituitarism in a boy of sixteen, presenting all the stigmas of gigantism, is reported because of a unique accompanying condition, a hemorrhagic osteomyelitis of a metacarpal bone. The family history is not relevant. The bone changes in perverted pituitary function are discussed briefly, and radiograms and measurements of this case are given. The hemorrhagic osteomyelitis cannot be definitely aligned with the pituitary disturbance, but is considered suggestive in view of the findings of other workers.—W. M. A.

The variability of the action of HYPOPHYSIS extract (Sur la variabilité d'action des extraits hypophysaires). Parisot (J.) & Mathieu (P.), J. de physiol. et de path, gén. (Par.), 1920, **18**, 1182-1193.

Small and large doses have opposite effects on involuntary muscle in general, including heart and blood vessels. The small doses cause excitation; the large doses inhibition. Therapeutic doses are excitatory.—Physiol. Abst., **6**, 73.

The influence of PITUITRIN on blood-sugar (Ueber den Einfluss des Pituitrins auf den Blutzucker). Partos (A.) & Katz-Klein (Freida), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **25**, 98-110.

When pituitrin is subcutaneously injected into rabbits there is produced a hyperglycemia and an increase in the water content of the blood. The point of attack of pituitrin is the periphery. The drug

acts as a retardant to **adrenin** hyperglycemia only to small degree. This is attributable in part to the alteration in the dry matter content of the blood. Pituitrin does not inhibit the **hyperglycemia** produced by theo-bromine.—F. S. H.

The influence of the HYPOPHYSIS upon growth; pathogenesis of acromegaly and gigantism (Ueber die Wachstumfunktionen der Hypophyse. Die Pathogenese der Akromegalie und des Gigantismus). Petényi (G.), Fortschr. d. Med. (Leipz.), 1922, **40**, 213-217.

Before the epiphyses are closed two kinds of growth disturbances may develop: (1) acromegaly without increase in length growth; (2) hypophyseal gigantism without symptoms of acromegaly. This makes it probable that the influence of the pars anterior of the hypophysis in bone growth is complicated. There probably exists an influence on the enchondral growth and, independent of this, an influence on periosteal growth. Both functions may undergo separate pathological changes. Increased periosteal growth produces acromegaly; increased enchondral growth, gigantism. If both functions are increased a mixed form develops.

—J. K.

HYPOPHYSIS in acute infectious diseases (Hypophysenbefunde bei akuten Infektionskrankheiten). Plaut (A.), Klin Wchnschr. (Berl.), 1922, **1**, 552.

Out of 35 cases of pyemia the hypophysis was affected 17 times. The changes in the posterior lobe were generally inflammations, in the anterior lobe necrosis. Acute meningitis rarely affects the hypophysis. In influenza and diphtheria no changes were found in the hypophysis.—J. K.

Respiratory metabolism in diseases of the HYPOPHYSIS (Gaswechsel bei Hypophysiserkrankungen). Plaut (R.), Klin. Wchnschr. (Berl.), 1922, **1**, 552.

A meal of 200 gms. meat, 50 gm. fat and 200 gm. bread causes an originally normal basal metabolism to rise 25 to 35%. In diseases of the hypophysis this rise is only ± 11%. Cases of adiposity with the same metabolism are probably of hypophyseal origin.—J. K.

X-ray treatment of the HYPOPHYSIS and HYPOPHYSEAL infantilism (Hypophysenbestrahlung und hypophysärer Infantilismus). Poos (F.), Klin. Wchnschr. (Berl.), 1922, **1**, 836-840.

Fränkel and Geller have exposed the hypophysis of young female rabbits to x-rays and have observed that the **generative organs** remained small. They concluded from this that x-rays influenced the generative organs via the hypophysis. Poos has carried out the same experiments with the same results. When, however, a leg,

for instance, is exposed to x-rays the effects are the same. When any organ is exposed to x-rays there is always a pathological change in all radiosensitive organs.—J. K.

(HYPOPHYSIS) Malformations of the pars nervosa and infundibulum (Gewebsmisbildungen in der Neurohypophyse und am Infundibulum). Priesel (A.), Wien. kiln. Wchnschr., 1922, **35**, 285.

The author observed little nodules of large cells with much protoplasm in the neurohypophysis and in the infundibulum. The cells were epithelial-like, polygonal with indistinct walls; from time to time they showed other forms. The nodules were small, though they might reach the size of a pin head. Once a tumor the size of a pea was found. It is probable that these nodules were congenital malformations.—J. K.

HYPOPHYSEAL dwarfism (Ein Beitrag zur Kentnis des hypophysären Zwergwuchses). Priesel (A.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67**, 220-274.

A man 91 years of age, 132 cm. tall, of good intelligence, never married. Autopsy showed developmental defects and tumor of the epithelial lobe and persistent cranio-pharyngeal canal. The skeleton is described. A careful histological study was made of the other endocrine organs also.—W. J. A.

Stimulative radiation of the HYPOPHYSIS (Reizbestrahlung der Hypophyse). Rahm, Klin. Wchnschr. (Berl.), 1922, **1**, 755.

A short note. This treatment in young rabbits increases weight.—J. K.

The casuistics of tumors of the HYPOPHYSIS (Beitrag zur Kasuistik der Hypophysentumoren). Roth (H.), Beitr. z. path, Anat. u. z. allg. Path. (Jena), 1920, **67**, 309-328.

Description of a case, including clinical, gross and microscopic findings.—W. J. A.

Cachexia and tuberculosis of the HYPOPHYSIS (Kachexie bei Hypophysentuberkulose). Schneider (H.), Klin. Wchnschr. (Berl.), 1922, **1**, 1027.

A girl of 18 suffered with osteomyelitis, after which she became cachectic, with slight symptoms of **thyroid** insufficiency. She had infantile sexual organs. The radiogram showed a small sella turcica. The tuberculin recation was positive and a röntgenogram of the lungs showed enlarged glands. Her case was diagnosed as tuberculosis of the sella turcica and hypophysis. **Organotherapy** was not successful.—J. K.

PITUITRIN. Selhorst (J. F.), Vox med. (Utrecht), 1922, **22**, 51-53.

An answer to Kouwer (see Endocrinol., 1922, **6**, 156) defending pituitrin. It is an extremely useful substance in obstetrics.
—J. K.

Secretory processes in the HYPOPHYSIS (Contribution à l'étude des processus de sécrétion dans l'hypophyse). Stewart (F. W.), Arch. de Morph. gén. et expér. (Par.), 1922, **1**, 46.

Castration in the rabbit does not produce any change in the structure of the anterior lobe of the hypophysis. The author states that many methods for staining the sections of the hypophysis are defective. In the sinus and the intercellular spaces of the anterior lobe, cells are found, derived from the blood preparing organs. They are formed partly by the connective tissue of the sella turcica. A very large number of these cells is found in this connective tissue and in its vessels. It is sometimes possible to see in the sections how these cells are digested—by phagocytosis by the cells of the hypophysis. These cells play no role in the hypophysis. The cells of the anterior part of the hypophysis are all of the same sort. The cells are first basophilic and gradually become eosinophilic. Often eosinophil granulations are found in the intercellular spaces. The last stage of the cell is when its border is formed by an eosinophil ring; this ring gradually disappears, the cytoplasm becomes once more basophilic, and a new cycle of secretory activity begins. Pycnosis of nuclei generally is a symptom of degeneration. However, it may indicate also exhausted cells. In this case, after some rest, the cell and the nucleus regain their normal appearance.
—J. K.

Oxytocic substances in posterior lobe of the HYPOPHYSIS (Ueber den Gehalt der Hypophysenhinterlappen—Extrakte an uteruserregenden Substanzen.) Trendelenburg (P.), München. med. Wchnschr., 1922, **69**, 106-107.

Comparison of some commercial preparations.—J. K.

A case of HYPOPHYSEAL nanism (Über einen Fall von hypophysärem Zwergwuchs). Witthauer (W.), Klin. Wchnschr. (Berl.), 1922, **1**, 998.

The author describes a man of 24 years, 1.36 cm. in height, who had ceased to grow when he was 6 years old. He never perspired; he was quite normally proportioned; he had no pubic or axillary hairs; his voice was infantile; **diabetes** was not manifest and he was very intelligent. Radiograms showed a very large sella turcica and open epiphyses of all bones. His **carbohydrate** tolerance was high. Injection of **adrenalin** had almost no influence on the blood pressure and did not produce glucosuria. Abderhalden's reaction was positive with **testicle, adrenal** and hypophysis. The disease is probably caused by hypofunction of the pars anterior of the hypophysis.—J. K.

Ergot, quinin and PITUITRIN. Wright (A. H.), Canad. M. Ass. J. (Montreal), 1922, xii, 383-386.

Of no endocrine interest.—J. H.

Action of INTESTINAL extract and extracts of other organs on the bronchial musculature and the pulmonary circulation. Hallion (L.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 358-368.

Extracts of intestinal mucosa exert a broncho-constrictor effect, and varied but characteristic responses in the circulation. With the exception of renal extracts the results with extracts of other organs were found to be quite comparable.—Chem. Abst.

LIPODYSTROPHIA progressiva. Reuben (M. S.) & Zamkin (H. O.), Arch. Pediat. (N. Y.), 1922, **39**, 112-116.

Report of two cases in girls of 10 and 12 years of age with no symptoms referable to glands of internal secretion. X-ray examination of both skulls were negative. A short bibliography on the subject is appended.—M. B. G.

MONGOLIAN IDIOCY in one of twins. McLean (S.), J. Am. M. Ass. (Chicago), 1922, **78**, 13-15.

A mongolian idiot with a normal twin sister is evidence against any endocrine disturbance or general condition in the mother being an etiological factor. The author suggests that in this case an abnormality in one of a pair of germ cells may be responsible. A brief reference is made to the interest of endocrinologists in mongolian idiocy.—W. M. A.

Notes on MONGOLISM. Thursfield (H.), Brit. J. Child. Dis. (Lond.), 1921, **18**, 18-21.

Basing his studies upon 42 mongolian idiots which he was able to observe for a number of years, Thursfield concludes that there is no proof that the mongolian is the last of a long family or that he is born at the end of the child bearing period. Health during pregnancy and the difficulty of the labor had no influence on the production of mongolianism. The incidence of previous miscarriages in the mother was also small as only 19 of the 42 gave such a history. Tuberculosis and syphilis and other infectious diseases apparently do not play much of an etiological role, but prevention of conception or measures at attempts may have some bearing. He found that 7 of the 42 mongolians had cardiac defects. Incurving of the last phalanx of the little finger was found in 13, absent in 16 and not noted in 13. The fissured tongue was not present in the first few months of a child's life, at least not before 12 months. In the author's experience, speech, general in-

telligence, obedience and even temper seemed to be promoted by the use of thyroid extract. Mentality was not so amenable to treatment.—M. B. G.

ORGANOTHERAPY (Uber Organotherapie). Biedl (A.), Ztschr. f. ärztl. Fortbild (Jena), 1922, **19**, 161-167.

An admirably conservative lecture delivered by the author before a medical gathering in Berlin. The best example of logical and intelligent organotherapy is the administration of **thyroid** in **cretinism** and **myxedema.** Kocher has stated that after complete thyroidectomy the patient remains perfectly healthy if he receives thyroid preparations regularly. The author, however, believes that though this treatment is exceedingly useful, it is not completely adequate. Since we do not know any good way of standardizing thyroid preparations exact dosage is nearly impossible. Perhaps Kendall's thyroxin will prove of great use in avoiding this difficulty. As nearly all endocrine diseases are pluriglandular, organotherapy is very complicated and often is less successful than would be expected. To have success with organotherapy an exact study of the patient, of his "endocrine constellation" is necessary. A complete study of **metabolism** is also necessary in most cases; sometimes regular weighing of the patient is enough; but often an exact study of basal metabolism is needed. The author warns against our speaking of hyper- or hypo-function of an organ. As we do not know how to calculate the normal function of such a gland, these words indicate merely lack of physiological knowledge.

—J. K.

Division of work in the OVARY (Die Arbeitsteilung im Eierstock). Guggisberg (H.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 402-407.

The ovary has at least three functions. It produces ova, it produces hormones influencing the **secondary sex characteristics,** and influences metabolism,—especially **carbohydrate metabolism.** When castrated rabbits are injected with 0.05 mg. **adrenalin** the **blood sugar** increases; but when the animal is not castrated this reaction is not seen. The same results are seen after castration by radiation as by surgery. The animals become fat. The author has castrated the animals with x-rays and has examined the ovary some time afterwards. Changes in the interstitial cells were never seen. The follicles were severely degenerated. Therefore, he believes that the follicles have an influence on metabolism; if they degenerate, a change in metabolism occurs. Therefore it is believed that the follicles have an incretion and that the endocrin as well as external function of the ovary is due to the same elements.

—J. K.

Treatment of symptoms caused by loss of OVARY (Zur Therapie der ovariellen Ausfallserscheinungen.) Halban (J.), Klin. Wchnschr. (Berl.), 1922, **1**, 708.

Loss of the endocrine function of the ovary causes a hypersensibility of the sympathic. Organotherapy is not successful, but calcium, theobromin, and nitroglycerin are useful.—J. K.

Treatment of skin diseases of the menopause with OVARY (Ovarialtherapie klimakterischer Toxikodermien). Hofbauer (J.), Zentralbl. f. Gynäk. (Leipz.), 1922, **46**, 558-560.

Report of two cases of skin diseases (no exact diagnosis is given), cured by injections of ovoglandol. Liuthlen in Vienna has reported good results from injections of ovoglandol or **thyroid** and **hypophysis** extract in pruritus vulvae and pruritus universalis, acne rosacea, chronic eczema and dermatitis bullosa faciei. That the ovaries have a relation to the skin is proved by the cases of dermatitis symmetrica dysmenorrhoeica.—J. K.

True diffuse PANCREAS hyperplasia (Echte diffuse Pankreashyperplasie). Sklawunos (T. G.), Centralbl. f. allg. Path. u. path. Anat. (Jena), 1922, **32**, 260-264.

Sklawunos refers to the infrequency of hypertrophy of the pancreas and points out that the great majority of the cases have been seen in **acromegaly**. A case is reported which was not associated with this disease. The patient was a male, 58 years old, 170 cm. in height and 64 kg. in weight. He died of luetic aortitis, erysipelas and sepsis. The pancreas, stripped of all adventitial tissue, weighed 182 gms. (normal average 83.5 gms.), and measured 25x6.5x3 cm. (normal average equals 18.4x5x2.5 cm.). The weight and dimensions were therefore at the upper border of physiological variation and in relation to body weight it was 0.28% as compared with the normal of 0.15%. The author states that there was a true hyperplasia of the gland tubules giving a relative decrease in the number of islands of Langerhans irrespective of the portion of the pancreas studied. He was unable to find a cause for the enlargement, as all the bile ducts, pancreatic ducts and intestinal mucosa were normal. There was a gastric ulcer which he thinks was of no significance. He refers to the possibility of congenital hypertrophy similar to that seen in the spleen, **thyroid**, mammary glands, etc., and also discusses the possibility of its being an acquired compensatory hyperplasia due to some deficiency of digestive enzymes.—D. M.

PARATHYROID transplantation (Epithelkörperchentransplantation). Eden, Klin. Wchnschr. (Berl.), 1922, **1**, 1022.

A short note. Transplantation is recommended in cases of postoperative tetany.—J. K.

(PARATHYROID) The tetany syndrome and its pathogenesis (Das Tetaniesyndrom und seine Pathogenese). Frank (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 305-309.

A general review without new facts.—J. K.

(PARATHYROID) Studies on the pathogenesis of infantile tetany (Untersuchungen über die Pathogenese der infantilen Tetanie). Freudenberg (E.) & György (P.), Klin. Wchnschr. (Berl.), 1922, **1**, 222.

Will be published in detail in Jahrb. f. Kinderh.—J. K.

(PARATHYROID) Severe tetany (Schwere Tetanie). Hohlbaum, Klin. Wchnschr. (Berl.), 1922, **1**, 399; München. med. Wchnschr., 1922, **69**, 332.

In a nurse of 22, suffering from severe tetany, the parathyroids were grafted from a woman who had just died. The day after the operation there was a slight attack; then for 3 weeks, no attacks; increase of electrical irritability disappeared. Only the Chvostek symptoms were still positive.—J. K.

(PARATHYROID) Postoperative tetany and coma parathyreoprivum. Mann (L.) Zentralbl. f. Chir. (Leipz.), 1922, **49**, 548-549.

Administration of **thyroid** tablets in two cases of postoperative tetany caused one patient for 3 years, the other for 4 years to be free or nearly free from attacks. A third patient in whom strumectomy was performed with ligation of the 4 arteries fell into a coma resembling that of encephalitis. The tendon jerks were negative. Trousseau's symptom was slightly positive. Cure was effected by administration of thyroid (doses not given).—J. K.

(PARATHYROID) Tetany and hypertrophic cirrhosis of the liver (Tetanie bei hypertrophischer Lebercirrhose). Schur (N.), Klin. Wchnschr. (Berl.), 1922, **1**, 1028; Wien. klin. Wchnschr., 1922, **35**, 491.

The patient suffered from Hanot's cirrhosis and had typical attacks of **tetany**. This was probably due to parathyroid insufficiency. She had the same attacks when she fed a child.—J. K.

The pathology of the PINEAL gland: Epiphyseal adiposity with tumor-like degeneration of the organ (Zur Pathologie der Zirbeldrüse: Epiphysäre Fettsucht bei geschwülstförmiger Entartung des Organs). Löwenthal (K.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67**, 207-219.

A man of 23 years developed a pineal gland tumor the local symptoms of which were preceded for a considerable period by clinical manifestations including adiposity. The tumor had an epi-

thelial structure and clearly resembled the functioning (?) pineal of the newborn. It is held that hyperactivity of the pineal is responsible for epiphyseal adiposity.—W. J. A.

Secretin studies (Sekretinstudien, I, II). Eweyk (C. van) & Tennenbaum (M.), Biochem. Ztschr. (Berl.), 1921, **126**, 238-245.

Protein (casein) materials, after heating to 150-70°C., become secretin-containing, in the sense that they will cause the secretion of gastric juice in the Pawlow dog. This effect is due to the presence of histamine. It had been shown previously by Popielski that histamine would act as this type of secretin. The hormone from spinach is not histamine.—Med. Sc., **6**, 155.

The action of SECRETIN (L'action de la sécrétine). Halliburton (W. D.) & de Souza (D. H.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 231-241; abst. Physiol. Abst., **7**, 52.

In the preparation of secretin a boiling temperature is advantageous in that the coagulable proteins are eliminated; but one can very well operate at a low temperature. False secretin, an extract of spinach, or that which produces hydrolysed proteins, is not deserving of the name,—it is only slightly active and plays no role in digestion. Secretin injected by portal vein is less active than that injected by jugular vein, probably because in the first case there is more dilution in the blood.—F. A. H.

(SPLEEN) Pathology of polycythemia (Zur Pathologie der Erythraemie). Brieger (H.) & Forschbach (J.), Klin. Wchnschr. (Berl.), 1922, **1**, 845-848.

In polycythemia the number of leucocytes and platelets as well as the red cells may be increased. In some cases, the patient with polycythemia dies with all symptoms of leukemia. When the spleen is removed the number of red corpuscles is temporarily increased. A case is reported in which this operation was followed by polycythemia and a very large number of leucocytes. It is probable that the spleen controls the action of the bone marrow. Polycythemia is also seen in cases of endocrine disturbances, especially in **dysthyroidism.** This kind of polycythemia, however, differs from the cases mentioned above in that there is generally leukopenia with lymphocytosis.—J. K.

The relation of SPLENECTOMY to growth and appetite in the rat. Smith (A. H.) & Ascham (Leah), Am. J. Physiol. (Balt.), 1922, **60**, 250-254.

It has been repeatedly asserted that increased appetite and decreased activity result from removal of the spleen. The observations have been made usually without regard to accurate measurements or careful control of conditions. The authors used rats,

splenectomized at the age of 40 days. The controls were subjected to the traumatism of the operation without removal of the spleen. Osborne and Mendel's diet was given with the addition of 0.4 gm. dried brewery yeast to supply vitamine B. The observations extended over 43 weeks. The authors concluded that there is no evidence of increased appetite, no anaemia nor any departure from the normal rate of growth.—T. C. B.

Function of the SPLEEN under physiological and pathological conditions (Über die Funktion der Milz unter physiologischen Verhältnissen). Weicksel (J.), Ztschr. f. klin. Med. (Berl.), 1922, **94**, 90-100.

Of no endocrine interest.—J. K.

A case of TETANY after gastro-enterostomy (Auftreten von Tetanie im Anschlusz an eine Gastroenterostomie). Baumann (M.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 250-253.

Three days after a gastro-enterostomy for a stenosis of the pylorus typical tetany attack occurred, followed by another attack 10 days later. After this, no attacks were observed. Whether the **parathyroids** were factors is not known.—J. K.

Pathogenetic relations between TETANY and rickets (Pathogenetischen Beziehungen zwischen Tetanie und Rachitis). Freudenberg (E.) & György (G.), München. med. Wchnschr., 1922, **69**, 422.

The authors believe that symptoms of rickets always exist in tetany. The calcium content of the blood in rickets is normal, the phosphates are decreased. In manifest tetany the calcium is always low, the phosphates, normal or slightly increased. In the urine in rickets the quantity of phosphates and ammonia is high (acidosis), in tetany it is low (alkalosis). So there is a real contrast between rickets and tetany. When a patient with rickets gets tetany, it means that his acidosis is changed into alkalosis. The authors believe that this change can be accomplished by hormones. This is made probable by the fact that tetany generally begins or increases in spring, the season in which other endocrine conditioned processes, e. g., growth, are most intense. These facts are of importance for the treatment of tetany. All drugs or other treatments producing acidosis may be useful. NH_4Cl produces a rise in the excretion of phosphates, a phosphate diuresis with a calcium retention. Ingestion of acids and starvation tend to cure tetany.—J. K.

Spasmophilia and TETANY (Krampfbereitschaft und Tetanie). Gött (T.), Klin. Wchnschr. (Berl.), 1922, **1**, 553; München, med Wchnschr., 1922, **69**, 688.

Not of endocrine origin.—J. K.

Postoperative TETANY after goiter operations (Postoperative Tetanie nach Kropfoperationen). Knaus (H.), Beitr. z. klin. Chir. (Tübing.), 1922, **125**, 669-680.

In 619 operations for goiter 5 cases of tetany were seen. Two ended fatally. Three cases were seen after operation for a recurrent goiter. Knaus examined the removed piece of thyroid histologically. Parathyroids had been removed 21 times. No symptoms of tetany developed except in one case.—J. K.

Epilepsy in postoperative TETANY (Epilepsie bei postoperativer Tetanie). Koetzle (H.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 365-368.

A man of 20 underwent hemistrumectomy. Two years later a hemistrumectomy was performed on the other side. Three days after this operation tetany set in, followed by epileptic fits. Epilepsy has occurred in a few former cases after goiter operation. There is an interesting relation between epilepsy and the endocrine organs. —J. K.

Two cases of postoperative TETANY after removal of the THYROID (Zwei Fälle von postoperativer Tetanie nach Schilddrüsenexstirpation). Mann, Klin. Wchnschr. (Berl.), 1922, **1**, 550.

A short note without details In one case of resection of the thyroid with ligation of the 4 arteries the patient fell into coma parathyreopriva.—J. K.

Relations between the chemistry of the body and TETANY (Beziehungen des Chemismus des Organismus zur Tetanie). Orgler (A.), Klin. Wchnschr. (Berl.), 1922, **1**, 1023; München. med. Wchnschr., 1922, **69**, 451.

Tetany of infants largely depends on the food. Potassium and phosphorus increase the symptoms; calcium and magnesium have a good influence. In many cases the calcium balance is negative. The calcium content of the blood is low. Parathyroid tetany, guanidin tetany and spontaneous tetany of infants all show the same type of calcium metabolism.—J. K.

Serious TETANY after severe enteritis (Schwere tetanische Erscheinungen bei heftiger Enteritis). Severin, Klin. Wchnschr. (Berl.), 1922, **1**, 550.

In ± 10 cases the author observed tetany after enteritis and in one case after ileus. In these cases the tetany is latent.—J. K.

Anatomy of the THYMUS in rabbits of different ages (Zur Altersanatomie der Kaninchenthymus). Gedda (E.), Upsala Läkaref. Förh., 1921, **26**, 1-27; J. Aug. Hammer, Festskrift. Each article is paged separately.

The author has made an examination of the thymus gland from 124 rabbits of different ages. Most of the endocrine glands and the lymphoid tissue of the same animals were before numerically examined by Hellman and others. The curve indicating the weight of the thymus gland as a whole showed a considerable difference from the values noted by Söderlund and Backman in their early investigation, but those demonstrating the weight of the parenchyma showed a most remarkable resemblance. Hence, the difference in weight is due to the fat component and not to the parenchyma. The relation between the cortex and the medulla is not altered at different ages. Thus the thymus of the rabbit differs from the human thymus, showing a comparatively greater involution of the cortex. Probably this phenomenon is due to the general greater importance of the lymphocytes in the rabbit during all ages of life, proving that Hammar is right in asserting that the changes of the lymphocytes in the thymus gland are conditioned not by local but by general factors.
—H. B.

Microscopical analysis of the THYMUS in certain cases of congenital syphilis (Beiträge zur Konstitutionsanatomie VII. Mikroskopische Analyse der Thymus in einigen Fällen von Lues congenita). Hammar (J. A.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **66**, 37-81; 195-258.

An exhaustive review of the literature on the subject is given. A careful quantitative analysis is made of the thymus in a large number of cases of congenital lues. Percentages of volume are given for the cortex, the medulla and the Hassal's corpuscles, and these are compared with the normal percentages.—W. J. A.

Reaction of the THYMUS in acute infections: Microscopic analysis of the thymus in 21 cases of diphtheria (Verhalten der Thymus bei akuten Infektionen: Mikroskopische Analyse der Thymus in 21 Fällen von Diphtherie). Hammar (J. A.) & Lagergren (K. A.), Ztschr. f. ang. Anat. [etc.] (Berl.), 1918, **3**, 314-398.

The detailed data of an elaborate quantitative analysis of the thymus in 21 cases of diphtheria are given. In all of these cases except one, the whole organ and the parenchyma were below the average. The smaller Hassall's corpuscles were, on the contrary, strikingly increased. The interstitial tissue in 3 cases was above normal, in 10 cases within normal limits and in the other 8 cases below normal.—A. T. R.

La radiotherapie de la maladie de Basedow et des autres formes de l'hyperthyroidisme. Alschek (E.), These de Paris, 1920, 56 p.

This thesis reports 5 cases of exophthalmic goiter in which the x-ray treatment, using the Béclère technique, is stated to have brought about cure. The observations were made in the service of Dr. Béclère.—E. G.

(THYROID) Exophthalmic goiter and hyperthyreotoxic adenoma as two independent diseases (Der exophthalmische Kropf und das hyperthyreotoxische Adenom als zwei selbstandige Krankheiten). Bircher (M. E.), Schweiz. med. Wchnschr. (Basel), 1922, **52**, 347.

The writer—a Fellow in Medicine at the Mayo Clinic—summarizes the views concerning the nature and treatment of exophthalmic goiter presumably held by the staff of the Mayo Clinic. He outlines the several steps carried out in that clinic in the diagnosis, classifications, treatment and prognosis. Bircher states that more goiter cases are seen at the Mayo Clinic in two years than the late Professor T. Kocher saw in his entire lifetime and concludes the review by observing that it is remarkable that such high grade scientific work is being done in a country which half a century ago was a wilderness.—D. M.

(THYROID) Goiter prophylaxis (Zur Frage der Kropfprophylaxe). Bleyer, München. med. Wchnschr., 1922, **69**, 587-589.

The author first gives a short review of the geographical distribution of goiter in Bavaria and Switzerland. The increased number of goiter cases in Germany may perhaps be attributed to the fact that since the beginning of the war the importation of guano and artificial manure in Germany has ceased. The artificial mixtures that are now used are absolutely iodine free.—J. K.

(THYROID) Hereditary goiter (Erblichkeitsfrage des Kropfes). Bluhm (A.), Arch. f. Rassen-u. Gesellsch.-Biol. (Leipz.), 1922, **14**, 1.

There is a theory that all goiters, the endemic forms included, are typically hereditary diseases. Another theory, given by Siemens, is that endemic goiter is not hereditary, but that sporadic goiter is. Bluhm gives the genealogical tree of a family for four generations. This family seems to confirm Siemens' theory. In studying these questions it is of great importance to examine the so-called healthy members of a family and to note minor changes in the thyroid also.
—J. K.

Blood sugar after x-ray treatment of THYROID (Das Verhalten des Blutzuckers nach Röntgenbestrahlung der Schilddrüse). Brösamlen, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

Small doses of x-rays on the thyroid produce an increase, larger doses a decrease of blood sugar. In Graves' disease these effects are more marked than in healthy persons.—J. K.

THYROID function from a chemical viewpoint. Cameron (A. T.), Canad. M. Ass. J., 1922, **12**, 229-232.

A short account of our present knowledge of the chemistry of the normal and pathological thyroid in which the following points

are emphasized: the thyroid elaborates iodothyroglobulin, as the storage form of thyroxin, the necessary tryptophane and iodide being normally present in blood. Administration of iodine compounds is useful only in so far as iodide is set free. Thyroxin is not toxic in itself, but when present in circulating blood in amounts greater than normal causes undue tissue destruction and cell starvation and so acts as an indirect poison. For prolonged administration by mouth, desiccated thyroid seems more suitable than thyroxin, although it is essential that the iodine content be stated, since its thyroxin effect will be approximately proportional to its iodine content.—J. H.

(THYROID) The influence of war alimentation on Graves' disease (Sull' influenza dell' alimentazione di guerra sul morbo di Basedow). Curschmann (H.), Riforma med. (Napoli), 1922, **38**, 273-275.

From personal and other doctors' observations the author concludes that the period of hypoalimentation during and after the war has had an undeniably good effect on patients with Basedow's disease. The numerous cases of myxedema, rather frequent during the years of famine, and the accentuation of hypothyroidism strengthens his point. As a consequence, the author would suggest that not meat only, but any kind of meal giving too many calories, might induce hyperfunction of the thyroid and therefore render the condition in the Basedow patients worse. He suggests thorough research work in this field.—G. V.

The action of THYROID extract of a dog on the isolated heart of a normal or sensitized rabbit (Action de l'extrait thyroïdien de chien sur le coeur isolé du lapin normal ou du lapin sensibilisé). Demoor (J. O.), Arch. internat. de physiol. (Liége & Par.), 1921, **18**, 369-390; Abst., Physiol. Abst., **7**, 50.

The depressor action resulting from the addition of liquid thyroid extract of a dog to Locke's fluid perfused through the isolated heart of a rabbit is replaced by a pressor action if the rabbit has been previously sensitized by the intraperitoneal injection of thyroid extract. The author believes that immunity and anaphylaxis result from changes in the colloidal equilibrium of the blood or of the tissues.—R. G. H.

(THYROID) Serum concentration and viscosity of the blood in Graves' disease (Über die Serumkonzentration und die Viskosität des Blutes bei der Basedowschen Krankheit). Deusch (G.) Deutsches Arch. f. klin. Med. Leipz.), 1922, **138**, 175-180.

The viscosity of the total blood in Graves' disease does not show any typical change. In serious cases, however, the viscosity of the serum is decreased and its protein content, when tested with the refractometer, is low. The influence of treatment (operation, x-ray)

is seen by a rise of viscosity and a higher protein content of the serum. When thyroidin is given to healthy persons a lowering of viscosity and protein content of the serum may be found.—J. K.

A plea for early diagnosis and treatment of HYPERTHYROIDISM. Dowden (C. W.) & Enfield (C. D.), Kentucky M. J. (Louisville), 1922, **20**, 196.

Treatment of hyperthyroidism, to be entirely satisfactory, must be instituted in the earlier stages of the disease, before organic damage has been wrought. The bearing of the basal metabolic rate, the use of **adrenalin** (for observation of pulse, blood pressure and tremor), and the sugar tolerance test are discussed. The adrenalin test the author does not regard as useful. Vague and indefinite symptoms are also discussed. It is asserted by the writer that no medical treatment of hyperthyroidism has as yet stood the test of time. Surgery and roentgenotherapy are the only means of therapy that these writers regard as useful in this disease. Crile's summary of the relative advantages and disadvantages of surgical and x-ray treatment are discussed. A contrast is drawn between the period of incapacitation following surgery and the relatively very little time required for roentgenotherapy of this lesion. While Crile shows a one per cent death rate in his statistics, x-ray statistics show absolute lack of mortality applied to this particular treatment. Since many patients will not submit to surgical treatment, but will submit to x-ray in the early and curable stage of the disease, x-ray therefore could and does often prevent a fatal outcome in these particular cases. Also the authors favor roentgenotherapy because of the fact that it attempts to restore the normal thyroxin balance without a mass attack. If this attempt fails surgery is still an open recourse. The technique employed by these authors is as follows: The basal metabolism test, the Goetsch test and the sugar tolerance test are all made before x-ray is given. Three areas are treated, one on the right over the thyroid going to the middle line, similarly one on the left, and a third one over the thymus region. Eighty kv. (about eight and one-half inch spark gap), five ma., twelve inches anode-skin distance, four mm. aluminum and one cm. of sole leather, ten to fifteen minutes exposure at intervals of a week or ten days. Six such treatments are given unless the pulse drops rapidly after the first three or four treatments. After a period of two to three weeks the metabolic rate is again taken. If this is still high only a month's rest is given and a second series of similar treatments is then employed. Otherwise, a three months' period is allowed to elapse and the basal metabolic rate is then again determined. Complete cure, as far as symptoms and laboratory tests can determine, has been accomplished in some cases and decided relief has resulted in others. Case reports are appended.—J. Radiol., 1922, **3**, 253.

Direct continuity between PARATHYROID, THYROID and THYMUS in mammals (Sur l'existence de rapports de continuité directe

entre parathyroïdes, thyroïdes et nodules thymiques chez les mammifères). Dustin (A. P.) & Gérard (P.), Compt. rend. Soc. belge biol., 1921, **85**, 876-877.

The authors describe the existence in the cat of connections between thymic tissue, thyroid tissue and parathyroid tissue. This was formerly shown by Aimé and by Dustin in reptiles.

—Physiol. Abst.

Relations between intestinal movements and the THYROID (Ueber die Beziehungen zwischen Schilddrüse und Darmbewegung). Deusch, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

In chronic constipation there is often hypothyroidism. Administration of thyroid brings good results.—J. K.

(THYROID) Exophthalmic GOITER. Edmunds (W.), A lecture delivered at the North-East London Post-Graduate College, April 27, 1921; London, 1921, 1-34.

The loss of Ca which occurs both in Graves' disease and in **diabetes**, and the fact that Graves' disease is sometimes followed by diabetes, show that the two are related. A cure should be sought in both cases by the administration of Ca, or possibly of Sr.

—Physiol. Abst., **7**, 50.

(THYROID) Radical operation for Graves' disease (Radikaloperation der Basedowstruma). Els, Klin. Wchnschr. (Berl.), 1922, **1**, 549.

In extremely serious cases the author advises the complete removal of the thyroid and leaving a piece of gland the size of a cherry. It is rarely necessary to give thyroidin. Els operated upon 4 patients without tetany following. His results were very good.

—J. K.

Treatment of chilblains and chronic freezing with THYROID preparations (Ueber Behandlung der Pernionen und der chronischen Erfrierungen mit Schilddrüsenpraparaten). Embden (H.), München. med. Wchnschr., 1922, **69**, 201.

The author observed a patient with **hypothyroidism** who always suffered from chilblains. Administration of thyroid tablets had a good effect on the chilblains as well as on the hypothyroidism. He then tried this treatment in other patients with chilblains. In some patients the effect was excellent; other cases were not improved. It is not possible to tell beforehand in which cases treatment will give results.—J. K.

(THYROID) Goiter (Über den Kropf). Enderlen, Klin. Wchnschr. (Berl.), 1922, **1**, 457-461.

A general review without new data.—J. K.

(THYROID) The Roentgen treatment of morbus basedowii. Fischer (J. F.), Acta Radiol., 1921, **1**, 179.

In the beginning of his paper the author refers to the literature upon the subject of his paper, giving references. In all, he has treated 490 cases: 231 of these were private cases, of which a third were somewhat doubtful, a third slight, and a third severe cases of the disease. A case to illustrate the difficulty in diagnosis is given and discussed. Out of all the cases only 11 were of men. The majority of the patients were between 30 and 45 years, and the duration of the disease, for the most part, from 6 months to 5 years. Those treated at hospital and those treated privately were discussed separately as they are in different social positions, which is of importance. Those treated in hospital usually are laborers, and this increases the risk of contracting the disease. The method of treating private patients is given. Recurrence nearly always occurs in hospital cases, and the author states that this is due to overwork or domestic troubles. Taking the patients as a whole, four-fifths have benefited from the treatment and the remainder, even if no better, have not changed for the worse: only one patient died. Patients in whom tachycardia predominates over the nervous symptoms are those in whom x-ray treatment is most likely to fail. Fourteen cases are then described with moderately full notes and in each case at least two photographs are given, one before and one after treatment. According to the author, improvement begins after the first series of irradiations: weight should be observed, and in almost all cases where the patient is deriving benefit there is an increase in weight, often occurring about a month after the beginning of the treatment; though at first there may be a small loss. The effect of treatment on the various symptoms and the duration of benefit is related. Complications of x-ray treatment are next dealt with, particularly whether there is any danger to the patient; the author believes that there is none if treatment be carried out by skilled hands. The subjects which die are those in whom the disease is severe, and in them spontaneous hyperthyroidism may occur with no treatment, as is shown by a case quoted. It is not denied that in some circumstances x-rays may have an unfavorable effect. The author agrees with the vast majority that small doses are advisable in severe cases so as to avoid x-ray sickness; he quotes Nordentoft, who says that small doses would tend to cause hyperthyroidism, whereas large doses would not. The fact that the patient's skin is always very sensitive demands caution as a smaller dose than might be expected will often cause erythema. Various other possible complications are mentioned. The technique is then described. Author views the x-ray as far preferable to surgery, and says it should always be used unless there is a danger in putting off an operation which he considers to be a very rare event.—Med. Sc., **6**, 171-172.

(THYROID) Technique of goiter operation (Technik und Methodik der Kropfoperationen). Flörcken, Klin. Wchnschr. (Berl.), 1922, **1**, 876; München. med. Wchnschr., 1922, **69**, 526.

Of technical surgical interest.—J. K.

Treatment of the remainder of the THYROID after operations for goiter (Zur Stumpfversorgung bei Kropfoperationen). Flörcken (H.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 120.

Of technical, surgical interest.—J. K.

(THYROID) Frequency of goiter in school children in Munich (Kropfhäufigkeit bei Münchener Fortbildungsschülern). Fürst, München. med. Wchnschr., 1922, **69**, 156.

Kraeuter has shown that the number of girls with goiter in Munich has increased in the last years. In young individuals the author often observed a combination of underfeeding, goiter and **hypogenitalism.** He confirms the facts described by Kraeuter.

—J. K.

The influence of THYROIDIN on blood viscosity and serum concentration in healthy persons (Ueber den Einfluss des Thyreoidins auf die Blutviscosität und Serumkonzentration bei Gesunden). Frowein (B.), Ztschr. f. d. ges. exper. Med. (Berl.), 1921, **24**, 162-165.

When 0.1 thyreodin is given 3 or 4 times a day for periods of 2 or 3 weeks to healthy individuals the concentration of the blood serum is decreased and the viscosity remains the same. The effect on the serum concentration was determined by changes in the refractive index.—F. S. H.

(THYROID) A case of formes frustes of Graves' disease and a case of premenstrual goiter (Ein Fall von Basedowoid und ein Fall von pramenstrueller Struma). Gottlieb (K.), Wien. klin. Wchnschr., 1922, **35**, 402.

The author reports the case of a girl of 13 with nervous irritability, restlessness, gradually increased size of the neck, exophthalmos, perspiration, diarrhea and no menstruation. Graefe's symptom was positive in one eye. Another girl of 13 is also described who is restless and nervous and in whom a **goiter** is always seen before menstruation.—J. K.

(THYROID) Treatment of endemic goiter (Behandlung des endemischen Kropfes). Grassl, München. med. Wchnschr., 1922, **69**, 785.

In Bavaria an old popular remedy for goiter is cod-liver oil. Its good effects are probably due to its iodine content.—J. K.

Climatic treatment of THYROID diseases (Klimabehandlung der Schilddrüsenerkrankungen). Guhr, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 544; Klin. Wchnschr. (Berl.), 1922, **1**, 970; Wien. klin. Wchnschr., 1922, **35**, 533.

A short note. Patients with Graves' disease need a high mountaineous climate.—J. K.

(THYROID) Case of so-called metastasizing colloid goiter (Zur Kasuistik der sog. metastasierenden Kolloidstruma). Guth (K.), Zentralbl. f. allg. Path. u. path. Anat. (Jena), 1922, **32**, 257-260.

Guth reports the pathological findings in the case of a woman, aged 39, who died of generalized tuberculosis originating in chronic pulmonary tuberculosis. The thyroid gland was much enlarged, irregular in outline, and contained adenomata in both the lateral and median lobes. Some of these adenomata were hemorrhagic, others grayish-white, others grayish-yellow on section. Metastases were confined to a few nodules in the subperitoneal tissue in the region of the neck of the gall bladder. Microscopic examination of these metastases showed well differentiated thyroid alveoli containing colloid and similar in appearance to some of the adenomas found in the thyroid gland. He refers to Jaeger's four groups of metastasizing goiters, viz., (1) those in which the primary tumor and metastases are composed entirely of cancer tissue; (2) those in which the metastases showed both benign goiter tissue and cancer; (3) those in which it is difficult to determine what portion of the tumors are carcinomatous; and (4) those apparently benign goiters showing metastases with normal thyroid alveoli formations throughout. He refers to the famous Cohnheim case of a metastasizing colloid goiter, but does not mention von Recklinghausen's pertinent criticism.—D. M.

The role of the THYROID in heat regulation and fever metabolism (Zur Rolle der Schilddrüse für die Warmeregulation und den Fieberstoffwechsel). Grafe (E.) & Redwitz (von E.), Ztschr. f. physiol. Chem. (Berl. u. Leipz.), 1922, **119**, 125-138.

Fasted dogs were thyroidectomized and studied by means of the respiration calorimeter, when kept at temperatures of 14°, 20° and 27° to 30° C. The results of the investigation show that the loss of the thyroid did not seriously interfere with the chemical heat regulation of the organism. Only in the very small animals did cooling produce effects. One must, therefore, conclude that the thyroid is not as important a regulator of these processes as is generally believed. In only one dog was fever induced. The active agent was bac. suipestifer. Strange to say the dog lived. The metabolism increased markedly during the course of the fever.—F. S. H.

(THYROID) The operative story of goiter. Halsted (W. S.), Johns Hopkins Hosp. Bull. (Balt.), 1920, **19**, 71-257.

The author gives a complete review of the history of the operative treatment of goiter. He sketches briefly his own interest in the subject and states that in 1879-1880, while he was working in Vienna upon the thyroid gland in the fish, he does not recall seeing a single operation for goiter in Billroth's clinic. From 1880 to 1886 he saw only one such operation in New York, when he assisted at an operation in which the patient was in the sitting posture with a rubber bag tied round his neck to collect the blood, and at the operation only two artery forceps were in use. The article is a monumental work which gives a complete review of the literature on the subject, and includes no less than 375 references. The story of the modern technique is very largely traced by means of extracts from the various papers. The earliest account of an operation upon the thyroid is apparently that of Albucasis, which was performed somewhere about the year 330. From this time there was practically no progress with the exception of a few rather doubtful reports in the fifteenth, sixteenth, and seventeenth centuries, until the eighteenth century. It is of interest to note that in 1596 an attempt was made to remove a goiter from a ten year old girl. She died under the operation and the surgeon was imprisoned. A case reported by Gooch in 1770 was followed by severe hemorrhage, which was controlled by compression day and night for eight days by persons alternating with each other at the task. In the first fifty years of the nineteenth century about a hundred cases are quoted, but the mortality was extremely high and the operation was strongly condemned by such surgeons as Robert Liston, J. Dieffenbach, and S. Gross. A quotation from the last of these three throws a most interesting light upon the progress which has been made in the last sixty years, although it is too long to reproduce here. In 1869, Billroth had performed the operation twenty times with eight deaths, and it was his work especially that gave the impetus to this branch of surgery. The severity of the operations as carried out in this period, when there was no anaesthesia, when arterial forceps were not yet discovered, and when the tumor had reached an enormous size before surgery was considered, is well shown by the full account which is given of the operation performed by Dupuytren. Long and careful extracts are given of most of the reported earlier operations, and in the accounts of them all it is easy to realize how extremely dangerous and difficult the operation was. Apparently somewhere between 1877 and 1880 forceps first began to be used, with an immediate improvement in the results, which have now reached such a stage of perfection that it is indeed difficult to realize that the great danger of this operation used to be the absolutely uncontrollable hemorrhage. In 1879 a series of successful cases by Billroth was reported, and included sixteen in the antiseptic series. Of a total number in which he performed the operation in the pre-antiseptic era thirteen out of thirty-six died, whereas in the antiseptic period there were only four deaths in forty-eight cases.

Kocher's work commenced in 1874, and he was the first to realize that complete removal of the thyroid was followed by the disastrous results that are so clearly recognized today. His papers, which are fully reviewed by Halsted, show the enormous progress that has been made, especially in the treatment of exophthalmic goiter, and in 1895 Kocher was able to review his first thousand cases of operations for goiter. Halsted then reviews the progress of his own work in America, and gives an account of his own operation which is now so well known. This portion of the work is the most brief of the whole, and from it one would hardly appreciate that Professor Halsted has practically lived through the whole period of modern progress in these operations, and has indeed done so much to produce the successful modern results. Although so brief an abstract is alone possible, the article is the most complete which has yet been published. A full account of the progress of this branch of surgery is given with very complete abstracts of every paper of note.—Med. Sci., 1922, **6**, 37-38.

(THYROID) Goiter in children (Kropf bei Kindern). Hamburger (F.), Wien. klin. Wchnschr., 1922, **35**, 470; München. med. Wchnschr., 1922, **69**, 729; Klin. Wchnschr. (Berl.), 1922, **1**, 1236.

Goiter is not rare in children. It is nearly always a parenchymatous struma and often produces stridor. In infants it may produce symptoms of suffocation. As a child's neck is short, it is often difficult to feel the thyroid. In most cases 1 mg. of NaI, three times a week is sufficient treatment.—J. K.

The secretory action of the PANCREAS in relation to the THYROID gland. I. The effect of thyroid feeding in rats upon the secretory action of the pancreas. Hashimoto (H.), Am. J. Physiol. (Balt.), 1922, **60**, 357-364.

A continuation of the work reported previously (Endocrin., 1920, **4**, 56). Feeding large quantities of desiccated thyroid diminishes notably the amylase content of the pancreas. This may account for the digestive disturbances observed during thyroid feeding. On the contrary, small quantities cause a fair increase in function.—T. C. B.

The secretory action of the PANCREAS in relation to the THYROID gland. II. The effect of thyroidectomy in rats upon the secretory action of the pancreas. Hashimoto (H.), Am. J. Physiol. (Balt.), 1922, **60**, 365-370.

Pursuing his studies further, the author finds that removal of the thyroid in rats results in a decrease in secretory activity of the pancreas. From all his observations Hashimoto concludes that the thyroid secrets an excitatory autacoid maintaining the normal functioning of the pancreas.—T. C. B.

(THYROID) Pathological changes in the heart in exophthalmic goiter. Hashimoto (H.), Iji Shimbun, 1922, No. 1080; Jap. Med. World (Tokyo), 1922, **2**, 75.

The author produced interstitial myositis by feeding thyroid preparations. He believes that there are similar changes in Basedow's disease. In both they can be controlled and ameliorated by proper treatment. See Endocrin., **5**, 559.—R. G. B.

(THYROID) The present day sources of common salt in relation to health, and especially to iodin scarcity and goiter. Hayhurst (E. R.), J. Am. M. Ass. (Chicago), 1922, **78**, 18-21.

Many authors are quoted as to the distribution of iodine in nature, its scarcity in the present day dietary of man and animals, and the relation of this scarcity to goiter. The last is not discussed except to emphasize the scarcity of goiter in maritime districts as compared with inland regions. Iodine is present in very small quantities in the ordinary diet. Commercial preparations of common salt contain no iodine even though the original source may have done so. The methods of preparation remove all of it even when the salt is obtained from sea water. The sea is the great store-house of iodine and the author therefore strongly recommends that sea water itself or a "salt" containing all the sea salts be used as a condiment. This will furnish sufficient iodine as well as perhaps other valuable constituents.—W. M. A.

(THYROID) Light cases of hyperthyroidism (Die Hyperthyreosen leichteren Grades). Hellwig (A.), Beitr. z. klin. Chir. (Tübing.), 1922, **125**, 75-116.

An abbreviated version of the same article has been published in Deutsche med. Wchnschr. and previously abstracted.—J. K.

Radium treatment of changes in the THYROID gland. Heyerdahl (S. A.), Acta Radiol., 1921, **1**, 207.

Various authors are referred to who have used radium in preference to x-rays in treating thyroid lesions. Aitkins, of Toronto, is quoted as saying that in acute cases radium must be supplemented by rest in bed, diet, and drugs. Gamma rays alone are used. Aitkins' technique and the opinions of Claquett, of Chicago, are mentioned. The results of treating eight cases of plain goiter are given; in all the goiter was diminished and there was a change for the better. The inconveniences of the treatment and the danger of telangiectasis are dealt with. The author's opinion is that for this type of case radium will only be used when operation is out of the question. The technique is described. Eight cases of toxic goiter were treated, and the results and the effect of the treatment on symptoms are described. Detailed notes of eight of the sixteen above mentioned cases are given and followed by those of four out of

eight cases of struma malignum, of which five showed temporary improvement and three no improvement.—Med. Sci., 1922, **6**, 85-86.

Endocrinology and woman. The THYROID and circulation (Endocrinologie de la femme. Thyroïde et circulation). Ide (M.), Rev. méd. de Louvain, 1921, 389-395.

The author discusses the influence of the thyroid gland on the sexual function, the influence of the ovaries on the thyroid gland and the relations between the functions of the thyroid and circulation.—R. G. H.

(THYROID) Myxedema and Kaufmann's disease (Myxödem und Kauffmannsche Krankheit). Japha, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 681-682.

Demonstration of 3 patients with myxedema. All were treated with **thyroid**, but only one, a girl of 25, developed enough to earn her living by needle work. The two other patients are, though much improved, physically retarded. Good results may be expected only when treatment begins as soon as possible. A fourth case is also described, that of a girl of 9, closely resembling a case of myxedema. She was suffering from micromegaly due to chondrodystrophy (Kaufmann's disease).—J. K.

(THYROID) X-ray findings in the trachea, especially after goiter operation (Röntgenbefunde an der Trachea, besonders nach Kropfoperationen). Kästner (H.), Beitr. z. klin. Chir. (Tübing.), 1921, **122**, 455-474.

When a goiter has reached a certain size its pressure may change the position and the form of the trachea. The author found that after goiter operation the trachea quickly regained a position almost normal, and by a week after the operation its position was usually as nearly normal as it ever would be; an absolutely normal position often did not return. This is not astonishing since a certain degree of tracheomalacia often exists. The trachea often takes an abnormal place again some months or years after the operation. This is probably due to the formation of cicatrix.—J. K.

(THYROID) Goiter prophylaxis by means of iodin tablets (Zur Kropfprophylaxe durch Iodtabletten). Klinger (R.), Schweiz. med. Wchnschr. (Basel), 1922, **52**, 315.

The view seems to be spreading among medical men that sooner or later the prevention of simple goiter will be made general and automatic by the administration of iodin in table salt. But for meeting the present condition in school children where both prevention and therapy are necessary, tablets certainly have a great value. The author refers to "iodostarrin" tablets which he has used extensively during the last two years. While probably one milligram

of iodin administered weekly is sufficient in most cases, four milligrams weekly can do no harm and is an additional safety.—D. M.

(THYROID) Myxedema frustrum. Kowitz, Klin. Wchnschr., 1922, **1**, 397; Deutsche med. Wchnschr. (Berl.), 1922, **48**, 472.

No details are given. The patient was a man of 51 years and after treatment with thyroid tablets metabolism became normal. The excretion of water and salt, which had been defective before, became normal also.—J. K.

Importance of gas metabolism determination for THYROIDIN treatment (Bedeutung des Stoffwechsels für die Thyreoidintherapie). Kowitz, München. med. Wchnschr., 1922, **69**, 796; Klin. Wchnschr. (Berl.), 1922, **1**, 1280.

Merck's thyroid tablets increased metabolism always. The effect is most marked in **myxedema.** Patients with **dystrophia adiposo-genitalis** may show an increased sensitiveness to thyroidin.
—J. K.

(THYROID) The frequency of goiter in school children (Ueber die Verbreitung des Kropfes bei Schulkindern). Kraüter (J.), München. Med. Wchnschr., 1922, **69**, 47-48.

The prophylactic administration of small doses of iodine is recommended.—J. K.

Compensatory hypertrophy of the THYROID giand. Loeb (L.), Tr. Ass. Am. Physicians, **34**, 240-242.

See Endocrin., **6**, 357.

(THYROID, HYPOPHYSIS) Dercum's disease (Dercumsche Krankheit). Löning, Klin. Wchnschr. (Berl.), 1922, **1**, 973.

A short note. The skiagram of the skull was negative. Thyroid and hypophysis preparations were given without any success.
—J. K.

THYROID medication in certain nurslings of arrested development (La médication thyroidienne chez certains nourrissons arrêtés dans leur développement). Maillet (M.), Bull. gén. d. thérap. [etc.] (Par.), 1922, **173**, 214-216.

Maillet reports his results from treating 32 poorly developed infants of 20 months of age with thyroid preparation. The symptoms were apathy, hypotonicity, anorexia and vasomotor disturbances of the extremities. From 1 to 2.5 cgm. was the initial dose. The effects had to be watched very closely. Nervous conditions, insomnia and gastro-intestinal disturbances are contra-indications. The changes in psychic condition and muscular tonicity are to be studied rather than the weight change in determining the effect of the drug. The effects are observable in 8 to 15 days. The following

doses are usually the same as the initial dose, although judgment must be made. The drug is given for 10 days, stopped for 10 days and so on.—F. S. H.

(THYROID) Surgical treatment of congenital goiter in an infant (Zur Operativen Behandlung der Struma congenita des Säuglings). Melchoir (E.), Klin. Wchnschr. (Berl.), 1922, **1**, 472

Good results were obtained in a child of 7 months from an operation for cyanosis.—J. K.

(THYROID) Pregnancy in sporadic cretinism (Schwangerschaft bei sporadischem Kretinismus). Merguet, Klin. Wchnschr. (Berl.), 1922, **1**, 971.

A cretin of 28 years, who had not been treated, became pregnant. The child was born by cesarean section and died of unknown cause shortly after birth. The child appeared normal and had a histologically normal thyroid.—J. K.

(THYROID) The goiter problem (Zur Kropffrage). Miesbach (E.), Deutsche med. Wchnschr. (Berl.), 1922, **48**, 657-658.

In all mountainous countries a long distance from the sea, but especially in the Alps, the kitchen salt, the water and the plants contain very little iodine. This is the case in Bavaria. There are in Bavaria some sources with large amounts of iodine, but these sources have no influence on the composition of the drinking water; hence here goiters may be attributed to low iodine content of the water. Kocher has shown that the goiters in fish disappear when iodine is added to the water. The work of Marine in Ohio and Klinger in Switzerland has proved the vital importance of the administration of small doses of iodine in the prophylaxis of goiter. Kraeuter in Munich has advised giving small doses of iodine to school children. Miesbach considers it the duty of the state to carry out this simple prophylaxis.—J. K.

(THYROID) A case of retrosternal goiter (Ein Fall von retrosternalem Kropf). Molnár (A. L.), Klin. Wchnschr. (Berl.), 1922, **1**, 420.

Description of a case.—J. K.

Functional diagnosis of the THYROID (Funktionelle Diagnostik der Schilddrüse). Neuschloss, München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

In athyroidism the viscosity of the serum is largely increased. In Graves' disease the viscosity is slight.—J. K.

Basal metabolism study of a case of congenital myxedema treated with THYROID extract (Étude du métabolisme basal dans un cas de myxoedème congénital traité par l'extrait thyroidien). Nobé-

court & Janet (H.), Bull et mém. Soc. méd. d. hôp. de Par., 1922, **46**, 608-611.

A study of the basal metabolism of a 14 year old idiotic child weighing 26 kilos and 1.05 meters tall. The tissues were infiltrated, the skin was dry, the face moon-like. Thyroid opotherapy had produced no benefit. Nevertheless the administration of thyroid extract (dose or preparation not given) did raise the basal metabolism from the low point of 37.8 to a high value of 52.8.—F. S. H.

(THYROID) Goiter prophylaxis (Zur Kropfprophylaxe). Oswald (A.), Schweiz. med. Wchnschr. (Basel), 1922, **52**, 313.

Oswald summarizes the work of the American observers and states that his position regarding the use of iodine has been misinterpreted, in that he is not opposed to the use of iodine in goiter, but that it should be used with great caution and in very small doses. He refers to Klinger's use of iodostarrin tablets, but prefers to use one to two milligrams of sodium iodide weekly in schools. This is a very simple and exceedingly cheap procedure. He reviews the possibility of other vehicles of administration of iodine as candies, salt, etc., and states that desiccated thyroid in exceedingly small doses is highly efficacious but too costly for general use. (It might also be stated that it is too dangerous to be recommended for goiter prevention generally.) He believes that the work thus far accomplished brings the prevention of goiter within the reach of possibility. Whether the administration of iodine will succeed in entirely eliminating goiter is a question which will have to be decided by future generations. It is certain, however, that endemic goiter will be greatly reduced and in this direction much has already been accomplished.—D. M.

The oculo-cardiac reflex in HYPERTHYROIDISM and experimental hypothyroidism in the rabbit (Le réflexe oculo-cardiaque dans l'hyperthyröïdie et l'hypothyroïde expérimentales chez le lapin). Parisot (J.), Richard (G.) & Simonin (P.), Compt. rend. Soc. de biol. (Par.), 1922, **86**, 593-594.

In the normal rabbit, compression of the eye causes a slowing of the pulse, varying with the subject, from 8 to 20 pulsations. A single intravenous injection of 0.5 gm. of thyroid extract causes an exaggeration of the reflex. After a series of ten subcutaneous injections in twenty days, the reflex is very much less or slightly inverted. After thyroidectomy there is an exaggeration of the reflex followed in ten seconds by a secondary acceleration of the pulse for thirty seconds or more. The same is true for incomplete thyroidectomy. In thyroidectomized animals, compression thirty seconds after the intravenous injection of 0.5 gm. thyroid extract causes a slowing of the pulse, but less marked than the preceding; the secondary phase of acceleration is not marked. Injection of adrenalin sup-

presses or inverts the oculo-cardiac reflex during the phase of excitation of the sympathetic, but the reflex reappears slightly after return of the blood pressure and pulse to normal.—T. C. B.

(THYROID) Incomplete form of myxedema (Über inkomplette Formen des Myxödems). Perl (J. E.), Ztschr. f. ges. Neurol. u. Psych., 1921, **71**, 268; abst., Monats. f. Kinderh., 1922, **22**, 758.

Perl discusses several cases of what Hertoghe has called benign chronic hyperthyroidism. There are found in various combinations obesity, dermatitis, loss of hair, general trophic and menstrual disturbances. Thyroid therapy was followed by rapid amelioration.
—R. G. H.

(THYROID) Basal metabolism and ideal weight and pulse ratio as shown by the findings in more than twenty-five hundred observations on about twelve hundred subjects: A preliminary report. Peterson (Anne) & Walter (W.), J. Am. M. Ass. (Chicago), 1922, **78**, 341-343.

Interesting tables and diagrams embodying the investigations suggested in the title lead the authors to the following conclusions. Basal metabolism determination by tried out portable apparatus is reliable as checked by the closed circuit, gas analysis method. The mass of evidence is against weight being influenced to any consistent degree by **thyroid** activity alone. The pulse rate and basal metabolism are closely associated generally.—W. M. A.

The Kottmann reaction for THYROID activity. Petersen (W. F.), H'Doubler (F. T.), Levinson (S. A.) & Laibe (J. E.), J. Am. M. Ass. (Chicago), 1922, **78**, 1022-1023.

Kottmann's serum reaction was carried out on four hundred cases, made up of hyperthyroid cases, miscellaneous diseases and normal controls. Typical retardation of the reaction is given by over ninety per cent of the hyperthyroid cases and is very seldom found in other conditions. Border line cases were not available. The authors recommend the test as of clinical value.—W. M. A.

Influence of the spleen, kidneys, and THYROID on anaphylactic shock (L'influenza della milza, del rene, della tiroide nella produzione della crisi anafilattica). Pistocchi (G.), Pathologica (Genova), 1920, **12**, 239-240; Arch. per le sc. med. (Torino), 1921, **44**, 91-123.

With beef serum as antigen, neither preceding splenectomy nor nephrectomy influenced definitely the anaphylactic picture in the guinea pig. Removal of the thyroid, however, diminishes the sensitivity of the animal to the anaphylatoxin.—Chem. Abst., **16**, 1459.

(THYROID) Congenital goiter. Report of four cases. Porter (W. B.) & Vonderlehr (R. A.), Am. J. Dis. Child. (Chicago), 1921, **22**, 477-481.

The authors report four cases of congenital goiter in boys, aged 3½, 6, 8 and 14 years, occurring in the southwestern part of Virginia, where goiter is endemic. In the first case only did the mother of the child have a goiter. None of the boys presented any symptoms of either hypo- or hyper-thyroidism, any mental aberration or abnormal development. Especially noted was the lack of any toxic or pressure symptoms. All the goiters were symmetrically enlarged, the most prominent part being the isthmus. The consistency of the enlargement was soft but suggestive of the colloid type. Ascaris lumbricoides was found in the stools of all of the children.—M. B. G.

HYPERTHYROIDISM in puberty (Das Pubertätsbasedowoid). Pototzky (C.), Deutsche med. Wchnschr. (Berl.), 1921, **47**, 96-97.

Between the harmless swelling of the thyroid in puberty and real Graves' disease the author describes the "Hyperthyroidismus pseudochloroticus." Here we find a soft, large thyroid, a pale color and complaints of fatigue, but without chlorotic changes in the blood. Between this and Graves' disease the author describes "Pubertätsbasedowoid." Both "hyperthyroidismus pseudochloroticus" and "Pubertätsbasedowoid" are seen much more in girls than in boys. In the latter case there is a certain degree of exophthalmos, but no tachycardia. Nervous complaints, abdominal pains, restlessness, insomnia and perspiring are very frequent. Often these symptoms disappear with the onset of menstruation. Treatment with iron or arsenic is not successful. Good effect is seen from the ingestion of **ovarian** preparations.—J. K.

(THYROID) A case of intratracheal struma (Ein Fall von Struma intratrachealis). Puhr (L.), Klin. Wchnschr. (Berl.), 1922, **1**, 875.

A short note without details.—J. K.

(THYROID) Hypothyroidism. Rietschel, München. med. Wchnschr., 1922, **69**, 180.

A boy of 15, 109 cm. in height, with a good intelligence, had symptoms of myxedema and retarded ossification of the metacarpal bones.—J. K.

(THYROID) The physiology of hibernation (Ein Beitrag zur Physiologie des Winterschlafes). Schenk, Klin. Wchnschr. (Berl.), 1922, **1**, 659; München. med. Wchnschr., 1922, **69**, 530.

During hibernation animals have a low respiratory quotient. The same is seen in rabbits after thyroidectomy. Injections of thyroid, **thymus** or **adrenals** increases metabolism in such a way as to

awaken them. Animals that hibernate have an endocrine system that easily becomes insufficient and causes them to become lethargic when exposed to very low or to very high temperatures.—J. K.

Influence of the THYROID on creatin and creatinin metabolism (Der Einflusz der Schilddrüse auf den Kreatin-Kreatiningrundumsatz). Schenk (P.), München. med. Wchnschr., 1922, **69**, 797; Klin. Wchnschr. (Berl.), 1922, **1**, 1281.

After ablation of the thyroid in rabbits less creatin and creatinin is excreted. After administration of extract of thyroid the secretion of creatin and creatinin is increased.—J. K.

(THYROID) A case of enormous goiter (Ein Fall von übergroszer Struma). Schloffer, Deutsche med. Wchnschr. (Berl.), 1922, **48**, 616; Wien. klin. Wchnschr., 1922, **35**, 261.

Demonstration of a case. No details are given.—J. K.

(THYROID) Technique of operation for goiter (Zur Technik der Kropfoperation). Schloffer (H.), Beitr. z. klin. Chir. (Tübing.), 1922, **125**, 249-269.

Of technical surgical interest.—J. K.

(THYROID) Sporadic cretinism and hypothyreosis (Sporadischer Kretinismus bei Hypothyreose). Schmincke, München. med. Wchnschr., 1922, **69**, 65.

No details are given.—J. K.

Functional study of the THYROID (Funktionsnachweis und Funktionsprüfung der Schilddrüse). Starlinger (T.), Wien. klin. Wchnschr., 1922, **35**, 473.

Herzfeld and Klinger have propounded a theory that the first product of decomposition of protein of the different organs is fibrinogen. In 15 cases Starlinger has compared the fibrinogen content of the blood in the arteries and veins of the thyroid. In hyperthyroidism the fibrinogen in the veins is diminished; in hypothyroidism it seems to be increased. Also the time necessary for the precipitation of the corpuscles ("Blutkörperchensenkungsgeschwindigkeit") is different in the arteries and the veins of the thyroid, and this difference seems also to depend upon the function of the thyroid. Therefore, it is possible that the study of colloid chemical differences between the arterial and venous blood of the thyroid is of great importance in investigating the activity of this gland. As 15 cases are too small a number for definite conclusions, the author intends to control and extend his series.—J. K.

(THYROID-GONADS) True dwarfism (Über echten Zwergwuchs). Sternberg (C.), Beitr. z. path. Anat. u. z. allg. Path. (Jena), 1920, **67**, 275-308.

Description of a number of cases of dwarfism. The different effects of thyroidism and hypothyroidism, and the altered structure of the testes are considered.—W. J. A.

Sensitiveness of the THYROID to ADRENIN and exposure to x-rays (Beeinflussung der Adrenalinempfindlichkeit durch Bestrahlung der Thyreoidea). Szegö, München. med. Wchnschr., 1922, **69**, 723.

The reaction after adrenalin depends upon the function of the thyroid. When the thyroid of persons with sympathicotonia is exposed to x-rays, no reaction is seen after the injection of adrenalin. —J. K.

(THYROID) Cases of Graves' disease (Tilfælde af Mb. Basedowii). Trier (K.), Hosp.-Tid. (Copenhagen), 1921, **64**, 48.

Between 1913 and 1920 Trier has treated about 200 cases of Graves' disease at the Röntgen department of the Rigshospital in Copenhagen. In the course of two months he has personally examined 88 of these patients, and he has received reports on several others. A comparison of the results showed that there was little to choose between giving: (1) small exposures over a considerable period; (2) small exposures over a considerable period, the thymus being included, and (3) big exposures, both the thyroid and thymus areas being included. Trier's opinion of the value of x-ray treatment is guarded; it may be an excellent supplement to general medical treatment, giving this in many cases just the support needed to tip the scales in the patient's favor. But it is not of epoch-making importance, and it seems to matter little whether the thymus is treated or not.—Med. Sci., **6**, 175.

Accessory THYROID growing in oesophageal lumen. Whale (L.), Proc. Roy Soc. Med. (Lond.), 1922, **15**, Sect. Laryngol., 7.

The aberrant thyroid was about the size of a cherry in a woman aged 58. It caused obstruction until removed.—Physiol. Abst., **7**, 50.

Water and salt metabolism during treatment with THYROIDIN and extract of OVARY (Beobachtungen des Wasser und Salzwechsels bei Thyreoidin und Ovarialextraktbehandlung). Veil (W. H.) & Bohn (H.), Deutsches Arch. f. klin. Med. (Leipz.), 1922, **139**, 212-234.

Thyroidin was administered and extremely exact examinations were carried out in two patients. Both gradually lost weight, though one much more than the other. There does not exist a parallelism between diuresis and loss of weight. The patient who lost comparatively little flesh showed a real polyuria. The quantity of nitrogen taken with the food was smaller than that excreted. The loss of weight was due only to an increased **protein metabolism.** In both cases the hemoglobin content of the blood remained un-

changed, though the amount of water of the blood was increased, as was proved by the determination of the amount of protein in the blood. The experiments show that the loss of weight during the first days is due to an increased loss of water and NaCl; later, however, only the increased decomposition of proteins causes loss of flesh. During these experiments the pulse rate is slightly increased; after some days of ingestion of thyroidin the blood pressure sinks. When **ovoglandol** is given hyperchloruria with polyuria and loss of weight is often seen. The serum then becomes poor in NaCl. These symptoms, however, are seen after some days and may be preceded by a gain in wight. The first day that ovoglandol is taken the excretion of NaCl is increased, either to a very slight or very marked degree, after which it is not always the same. When the ingestion of ovoglandol ceases, polyuria with a urine of normal concentration occurs. In this way much NaCl is excreted. The authors further point out how very small doses of thyroidin in **myxedema** or **athyroidism** may produce marvels, while much larger quantities of thyroidin have little or no effect in cases of so-called minor thyroid insufficiency. It is necessary to be very careful to make this diagnosis (introduced into pathology by Hertoghe). Even in complete athyroidism no adiposity is seen; therefore, the use of thyroidin in treatment of adiposity is explained by its influence on water and protein metabolism.—J. K.

(THYROID) Drainage nach Strumektomie. Vidakovits (C.), Zentralbl. f. Chir. (Leipz.), 1922, **49**, 157-161.

Of technical interest only.—J. K.

(THYROID) Treatment and prophylaxis of endemic goiter (Behandlung und Prophylaxe des endemischen Kropfes). Wagner-Jauregg, Wien. klin. Wchnschr., 1922, **35**, 369-370.

In **goiter** belts the government should supply to the public kitchens slat containing about 2 mg. of KI or NaI per kilogram NaCl.—J. K.

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